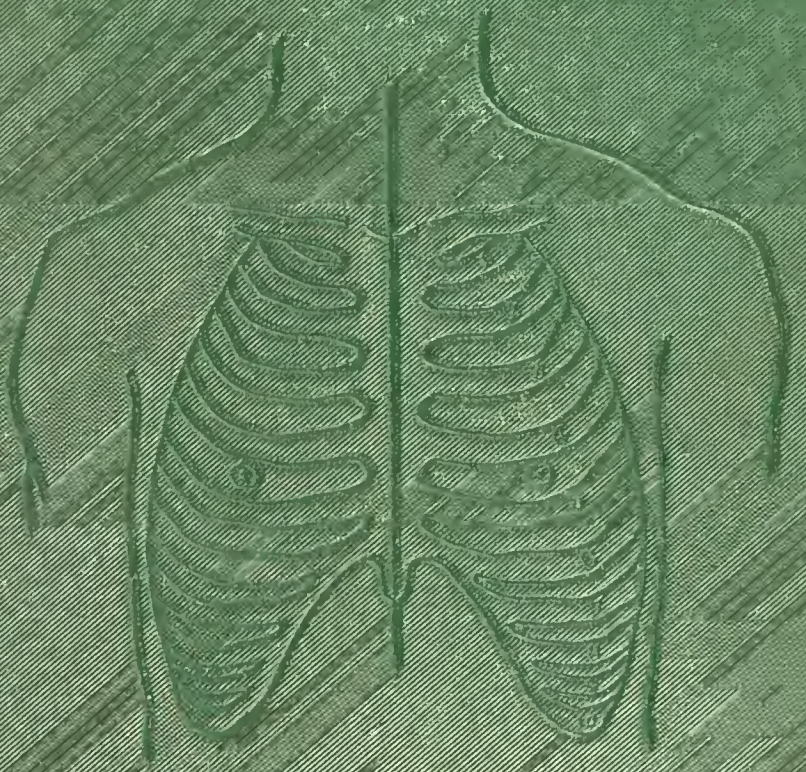
LETTSOMIAN LECTURES



DR SANSOM

THE TREATMENT

OF SOME OF THE FORMS OF

VALVULAR DISEASE OF THE HEART

BEING

THE LETTSOMIAN LECTURES

DELIVERED

BEFORE THE MEDICAL SOCIETY OF LONDON IN 1883

BY

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Second Edition, with Additions and Corrections

LONDON
J. & A. CHURCHILL
11 NEW BURLINGTON STREET
1886

PREFACE TO THE SECOND EDITION.

The First Edition of this work has long been out of print. As there have been notable advances in our knowledge of the pathology and therapeutics of diseases of the heart since the Lectures were delivered, I thought it might serve some useful purpose if I recast them and endeavoured to bring them up to date. Systematic works of high value bearing upon the subject have appeared since I addressed the Medical Society, notably the admirably illustrated treatise of Dr. Byrom Bramwell and the volume of Professor Oertel on Therapeutics. Our knowledge concerning ulcerative endocarditis and its relation to the ordinary forms of rheumatic endocarditis has been increased by the labours of Osler, Orth, Socin, Garrè, and others. Time, also, has been given for those definitely testing by clinical observation the value of remedial agents which at the time at which the Lectures were delivered were not commonly employed in this country. I have endea-

voured to present a summary of these advances in our knowledge, but I have omitted mention of new agents—possibly of great value—which have not yet been tested by clinical experience.

A. Ernest Sansom.

84, Harley Street, Cavendish Square,
London, *November* 1886.

PREFACE TO THE FIRST EDITION.

The Medical Society of London has honoured me by expressing the wish that these Lectures should be published. I comply with the request, regretfully conscious that much of imperfection attaches to them.

It was my intention to have included a brief sketch of the treatment of diseases of the aortic valves; I soon found, however, that this, to be consistent with my plan of exposition, was impossible. Such plan is mentioned at the commencement of my first Lecture, but I may add that I could not approach questions of treatment of any disease without formulating the bases on which I conceive such treatment should rest. To do otherwise would be, in my opinion, to promulgate an unscientific empiricism. In order, therefore, to define such bases for treatment I have been obliged to touch upon questions of pathology and diagnosis where I have considered that these have not been made sufficiently manifest by extant evidence. As far as possible I have avoided controversy, and have dealt with facts rather than with opinions.

The time allotted to me permitted, for the most

part, only a review of the indications for treatment of those diseases of the valves of the heart which are due to the form of endocarditis known as the rheumatic. To have followed my plan of exposition with regard to diseases of the aortic valves it would have been necessary for me to reverse the process—to have considered the diseases and disorders of arteries with their effects upon the aorta, and to have differentiated the centripetal or atheromatous from the centrifugal or endocarditic forms of disease involving the aortic valves. It is obvious that this could not be accomplished within the scope of these Lectures.

For the material of which I have availed myself I have to thank many kind friends: Dr. T. H. Green, who has permitted me to use some of his drawings, my colleagues at the London Hospital and the North-Eastern Hospital for Children, and the line of indefatigable House-Physicians, Medical Registrars, and Clinical Clerks at both these institutions.

Lastly, my thanks are due to the indulgent audience that made my task a pleasurable one.

A. Ernest Sansom.

81, Harley Street, W.
May 1883.

CONTENTS.

LECTURE III.

MITRAL STENOSIS.

THE

LETTSOMIAN LECTURES

ON THE

TREATMENT OF SOME OF THE FORMS OF VALVULAR DISEASE OF THE HEART.

LECTURE I.

ENDOCARDITIS.

The Rational Bases of Treatment—Morbid Anatomy—Exudative, Sclerous and Atheromatous Changes in the Endocardium—Ulcerative Endocarditis: its association with Micro-organisms—Clinical History of Endocarditis—Relation with Rheumatism, with Scarlatina and Measles—Rheumatic Endocarditis occurring without other manifestation of Disease—Endocarditis associated with Septicæmia; with Osteo-myelitis; with Ague; with Pneumonia—Pathogenesis—Perverted Metabolism as a cause of Rheumatic Endocarditis—Zymotic Causes inducing such Perversion—Micro-organisms determining the Necrosis in the Ulcerative Variety, but not initiating the Disease—Treatment of Endocarditis—Medication with Remedies for Acute Rheumatism—Preventive Treatment—Treatment of Severe (or Aberrant) Endocarditis.

In my first perplexity as to choice of a subject, when I learned that the Medical Society of London had done me the high honour of electing me Lettsomian Lecturer, I thought that I ought to be guided by two considerations. The first, that it behoved me to give of my very best—in other words, that I should

address you on a subject upon which I had the most personal experience. Yet I well knew that my best effort would fall far short of my desire and your deserving. The second, that, considering the character and traditions of this Society, I should aim at something practically useful. I am very far from decrying the labours of those who pursue Science for her own sake, and I well know that many who have done so have elicited truths which have eclipsed, in numberless instances, as regards importance and usefulness, the results obtained by those who might, from their mode of procedure, be deemed more practical men. But I dared not take a narrow path in mere hope. So I thought it best to review a subject which presents itself very frequently as a therapeutic problem to every one who is daily occupied in the practice of medicine, and I chose the affections which my title indicates because for many years my thoughts have turned towards them. It seemed to me that it might fulfil a useful purpose if I reviewed our extant knowledge as to the treatment of valvular diseases of the heart, compared these with the results of my own experience, and made, perhaps, a few suggestions as to progress towards precision in the future.

Then as to the point of view whence I could review the subject I felt some doubt. I could proceed from the therapeutic agent to the disease, or from the disease to the agent. Here, with all my difficulty as to how to perform my task, I could not hesitate as to how *not* to do it. I would by no means enunciate a therapeutic dogma, crystallize it into a phrase, and marshal the facts in such wise as they should support it, and if they refused—so much the worse for the facts. Apart from the consideration that such dicta

as "*Similia similibus curantur*," "*Contraria contrariis*," &c., present to my mind some of the most pernicious of hasty generalizations of our day, is the one consideration that they are based on the treatment of *symptoms;* and as I shall presently show that the diseases we are about to study are oftentimes accompanied by no symptoms at all, so the practical application of the dogma becomes an impossibility, and its universality an absurdity.

For many reasons I thought it best to consider the phenomena of disease first, and our treatment of them subsequently. My plan then will be to enunciate very briefly the bases on which I believe our therapeutics ought to rest. These are, in my opinion, (1) the teachings of morbid anatomy; (2) clinical observation of disease-processes and their correlations. Then I propose to review (3) the lessons of the past as to treatment, and (4) to adduce towards the elucidation of the various problems the arguments from analogy afforded by experimental investigation—a mode of inquiry rendered difficult, alas! by the stumbling-blocks which a false sentimentalism has placed in our way.

I. First, then, I will consider *the teaching of morbid anatomy as to lesions of the valves of the heart.* You will understand that I shall do this very briefly, for my object is merely to note them in so far as they may afford a guide to treatment, and when I speak apparently dogmatically I do not make an assertion *ex cathedrâ*, but in the spirit of an inquirer after truth.

We will first consider the disease which most commonly affects the valvular apparatus of the heart and the adjacent endocardium—the disease known

as *Endocarditis*. In briefly reviewing its morbid anatomy much will remain unsaid, but I shall treat it first from the standpoint of mere observation,

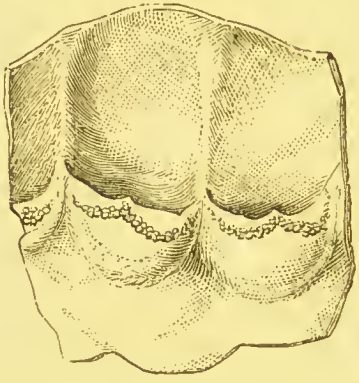

FIG. 1.—Inflammatory granulations on aortic cusps. (DR. GREEN'S *Pathology*.)

leaving all speculative questions. I would classify the *first* changes in the endocardium which I shall notice as *exudative*. The curtains or cusps of the

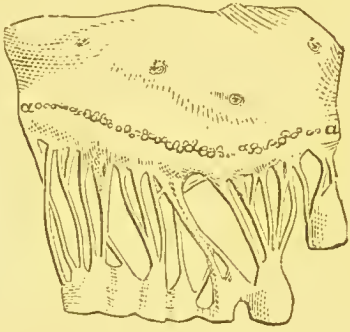

FIG. 2.—Inflammatory granulations on auricular surface of mitral curtains.—(DR. GREEN.)

valves may be seen to be slightly swollen, and the endocardium to contrast by its dulness with the healthy portions adjacent. The changes are most noticeable at the free edges of the valves, where may

be seen isolated or agglomerated beadlike processes. Upon such processes may be observed sometimes little caps of fibrin. The situations where these appearances are most obvious are (1) the line of contact of the aortic cusps at the time of their closure (Fig. 1); (2) the auricular aspect of the mitral orifice (Fig. 2). They are frequently seen also on the surface of the endocardium, in the neighbourhood of any abnormal thickening of, or growth upon, a valve (Fig. 3), and upon the chordæ tendineæ of the mitral.

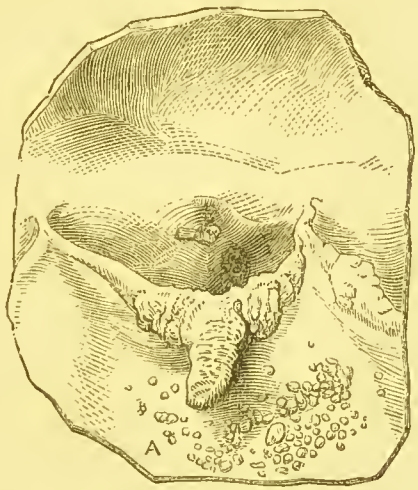

FIG. 3.—Inflammatory granulations in the neighbourhood of a large vegetation depending from an aortic cusp; these granulations probably induced by the mechanical irritation of such vegetation.—(DR. GREEN.)

A thin section of a valve thus affected is seen under the microscope to differ from healthy valve structure in that its cellular elements are more numerous, and especially towards the free edge are closely aggregated. I wish to insist on the fact that, in a valve so altered, even the portions which seem to the naked eye unaffected are really infiltrated with

cells. Only the aggregation is greater at the free edge, and here often the aggregated cells form little very slight concavities on which rest little caps of fibrin. The beadlike eminences observed by the naked eye are, then, according to my view, indications of a more widely spread inflammatory change in the valve than might be at first suspected. In a

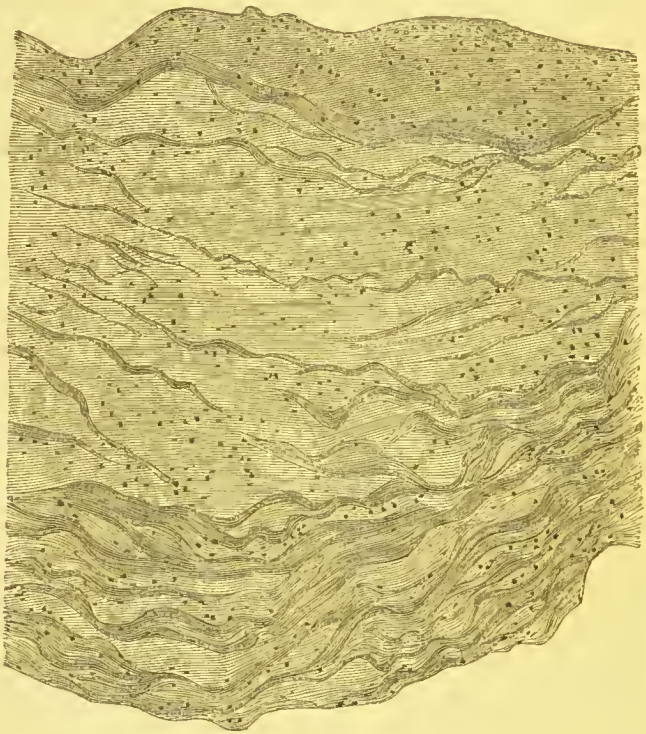

Fig. 4.—Section of Aortic Valve in a state of Health. (Hartnack, *Ob.* 3, oc. 3, 72 diams.)

microscopical section, which displays not only the inflamed valve, but the surrounding structures, one observes that as one approaches the inflamed valve, cells in number are scattered amongst the neighbouring muscular fibrillæ, and near the aortic valves the fibrous structures of the root of the aorta are similarly

infiltrated. The fibrous structure of the normal valve is rendered less evident, or is lost. The valve is swollen and infiltrated with cells. This is well shown by the accompanying drawings, taken from specimens prepared by my friend and colleague, Dr. Charlewood Turner. In the case of the healthy valve

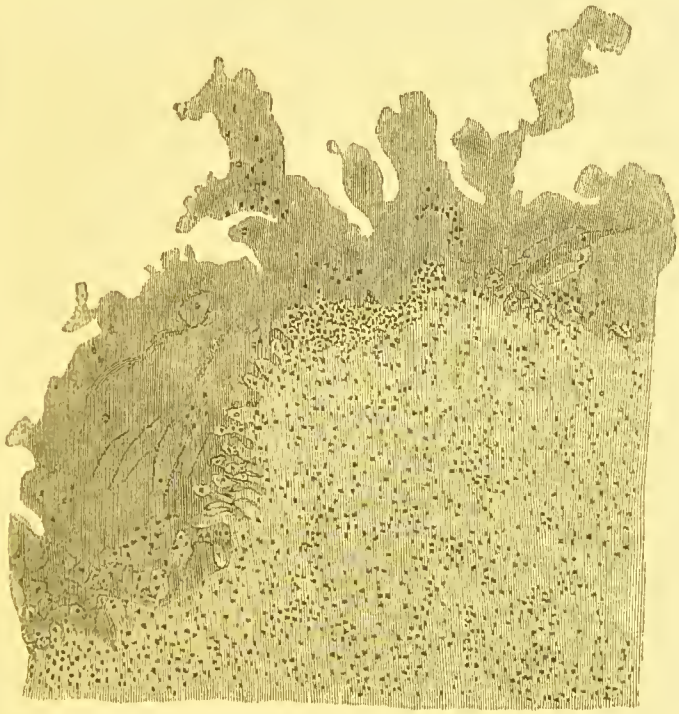

FIG. 5.—Section of Aortic Valve in a state of Inflammation, showing the free edge and a portion of the valve structure.—(Hartnack, *Ob.* 3, oc. 3, 72 diams.)

(Fig. 4) its whole thickness is shown. The drawing represents a portion of a transverse section of one of the semilunar cusps of the aortic valve near its attached border. The upper, or aortic portion, is seen to consist of a narrow band of compact fibrous tissue,

the fibrils of which are, for the most part, cut transversely. The lower or ventricular portion is of a looser structure, with its fibres parallel to the plane of section. Small, round nuclei are disseminated through the tissue. The specimen was taken from a well-developed woman, aged twenty-three. In the inflamed valve the increase of bulk is such that the artist cannot represent in reasonable space the whole of the section; the fibrous striation of the deeper portions is not visible, but cells are abundantly manifest throughout; at the free edge these cellular elements are aggregated at certain spots, and surmounting the margin is a fringe of fibrin. The specimen was obtained from a case of chorea, associated with endocarditis, in a girl, aged sixteen. It is scarcely encroaching on speculation if we conclude that this is the recent, the early stage of endocarditis. In looking over the records of sixty-eight post-mortems of cases of valvular disease at the London Hospital, I find that this stage of recent inflammatory change with exudation was observed in nine—*i.e.*, about 13 per cent. The aortic cusps were affected in five, the mitral in three cases. In one case mitral, aortic, and tricuspid were affected; in another, mitral, aortic, tricuspid, and pulmonic. In one case the tricuspid alone was thus diseased. In such early stage of endocarditis, emboli were noted in two cases —in one in the kidney, in the other in a branch of the pulmonary artery.

The *second form* of endocarditis, or properly speaking valvulitis, to which I shall call attention, is that which I would term the *sclerous* or fibrotic form. Here the valve—and it is the mitral which is affected in by far the greatest frequency—is thickened, but

the thickening is not due to swelling of the soft tissue; it is felt to be hard and firm. The endocardium of the auricle near the valve is found to be dense and white. The valve curtains, and often the cords and fleshy columns, are more or less rigid. A patch of the endocardium lining the left ventricle and leading up towards the aortic cusps is sometimes also found white and thick, and the aortic valves themselves may be seen to have undergone similar changes. In this form microscopic section shows that there is a gradual fibrous transformation of the neoplasm resulting in the production of a quasi-cicatricial tissue. In some cases the thickening is such that the structure resembles cartilage—in fact, Dr. Wilks has found well-marked cartilage in such a thickened mitral.* Or, degeneration continuing, calcareous change may take place, and the valve, &c., become of bony hardness. It is evident that this may be considered the chronic form of endocarditis. It was met with in one-fourth of the post-mortems in cases of heart disease which I have mentioned. The effects produced upon the mitral orifice will be treated of in future lectures. In this class of cases vegetations were observed in the proportion of seven instances in twenty cases—on the mitral and adjacent auricle in three cases, the aortic in two, the tricuspid one, the aortic, mitral, and tricuspid as well as in the auricle in one case. Infarcts were noticed in branches of the pulmonary artery (five cases), spleen (five), kidneys (two), brain (one), retinal artery (one), intestines (one).

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* "Pathological Anatomy," by Wilks and Moxon, second edition, p. 134.

A *third form* of endocarditis, which I think of practical importance to distinguish, is that which is *secondary to endarteritis* (atheroma). In this form it is the aortic valves which are affected in a large majority of instances. Patches of soft, flabby swelling may be seen in the lining membrane of the aorta close to the aortic cusps, involving them in the change, and perhaps causing the inversion of one or more. Or yellowish patches may be observed, in some cases covered by a soft pulpy material, the blood perhaps forcing its way at some softened spot between or within the arterial coats. Or the root of the aorta may be hard and thick, the thickening being of cartilaginous consistence, and in such thickening the cusps of the valve may be involved. Or in like situation and with like deformity of valves there may be a bony or stony hardness—a calcareous change. The evidence obtained by microscopic investigation is to the effect that in the swollen soft patches are abundant exudation-cells with hyaline or slightly fibrillar matrix. These occur mostly as swellings of the internal coat; but Dr. Wilks has observed them in all the coats of the vessel. The yellow patches show fat granules, and sometimes cholesterine crystals. There is evidently a fatty degeneration of the inflammatory neoplasm. In the fibrous or semi-cartilaginous variety we find more fibrillation and fewer cells; and in the hard and bony form there is a deposit of earthy salts in the interstices of the fibrous tissue. In this category came twenty-seven of the sixty-eight autopsies of heart disease which I have recorded. What I may term the *soft* stage was observed in eight instances, fibrous thickening in seven, calcareous change in five. The mitral valve was also thickened or

atheromatous in seven cases, the tricuspid in two. In one case where there was calcareous transformation, ulceration of one cusp of the aortic valve was also observed. Infarcts were discovered in three cases—less commonly, it will be observed, than in the other forms of valvulitis—in the kidney in one case, in spleen and kidneys in another, and in middle cerebral artery in a third.

The *fourth* and last form of endocarditis, as demonstrated by post-mortem examination, to which I shall call attention is that termed *ulcerative endocarditis.* Swollen and dull portions of the endocardium of the valve may be seen to present here and there a yellowish or greyish discoloration, and to be covered by a finely granular *débris.* The superficial endocardium in such situations has become necrosed. Through such breach blood may find its way, and, spreading between the layers constituting the valve, may form an aneurism thereof; or, the ulceration extending through both layers, the valve may be perforated. More commonly a considerable portion of the valve is eroded, and upon the eroded surface fibrin is deposited in the form of single or multiple vegetations. The finger readily detaches these vegetations, and the surface below them is found to be covered by a friable material. Microscopic examination has demonstrated in a very large number of cases the presence on the ulcerated surface and in the tissue of the valve of aggregations of micrococci. The accompanying engravings (Figs. 6 and 7), from preparations made by my colleague, Dr. Stephen Mackenzie, show the presence and positions of colonies of micrococci in ulcerative endocarditis, and the appearances of some of the detached masses (zoogloea).

Fig. 8 well shows the position of the colonies of micrococci upon a vegetation. The case was under the care of Dr. Sidney Coupland, of the Middlesex Hospital, who has kindly given me permission to reproduce the illustration, which, together with interesting details of the case, was published in the *Proceedings of the Medical Society of London* for 1885, p. 207. The micrococci chiefly occupy the surface of the vegetation, but they are also seen in the substance of the apparently homogeneous fibrinous deposit. Scattered chains and isolated micrococci are seen to have penetrated for a short distance into the basis of the vegetation, which is constituted of leucocytes and proliferated cells.

In this form of valvulitis embolism is the rule, and such emboli are sometimes *infective*—that is, they may lead to suppuration at the points whereat they lodge, or may be causes of septicæmia.

In the autopsies which I have taken as illustrative ulceration was observed in six. The ulceration affected the aortic valve in three cases, the mitral in two, and both aortic and mitral in one case. Infarcts were observed in five out of the six cases, the exception being in a case included under the category of atheroma, where one of the aortic cusps was destroyed by ulceration, the other being thick and calcareous. The infarcts were found in the spleen in three cases, the spleen and middle cerebral artery in one case, the spleen, middle cerebral artery, and kidneys in one case.

It may be asked whether by mere inspection the lesions of ulcerative endocarditis, the malignant endocarditis of Virchow and Osler, can be differentiated from those of the simple exudative or

papular form. I think so. In the case of the latter, the finger passed over the papules does

Fig. 6.—Vertical section through free edge of mitral valve in a case of Ulcerative Endocarditis. (*a*) Colonies of micrococci; (*b*) Corpuscular Infiltration (inflammatory). *Moderately magnified.* —(English, 2 inch o.g. 14 diams.)

not detach them, they are firmly attached to and in continuity with the endocardium; or if they be surmounted by fibrinous caps, these, though de-

tachable, are rather firmly adherent by their base, and when they are removed the papule presents no breach of surface. In the case of ulcerative endocarditis there is always some necrosis of the endocardium, the vegetations are friable, or, if large, are attached by a wide base, the surface left by their removal presents

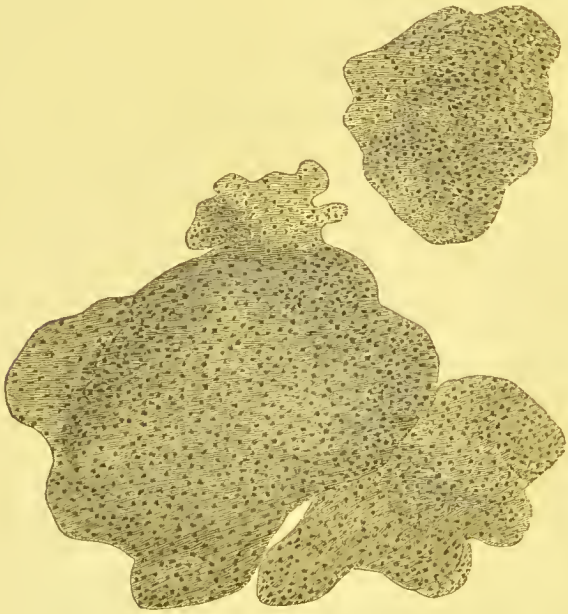

Fig. 7.—Colonies of Micrococci showing the spherules embedded in a mucous basis. *Highly magnified.*—(Hartnack, *Ob.* 8, oc. 3, 416 diams.)

the appearance of an erosion: the necrosis of tissue may be extensive and deep, the chordæ tendineæ may be attacked and destroyed, the valve-segments perforated, the heart muscle excavated. My colleague, Dr. Stephen Mackenzie, has recorded a case in which the left ventricle was perforated by the ulceration (*Path. Trans.* vol. xxxiii.). In other cases the necrotic process is accompanied by suppuration, small abscesses may be observed at the base of vegetations, or patches

of the endocardium may be found to have undergone suppuration. In some instances, Dr. Osler says, suppuration seems to be the initial stage in the endocarditis.

In a large majority of cases, at least seventy-five per cent., the ulcerative or suppurative processes are

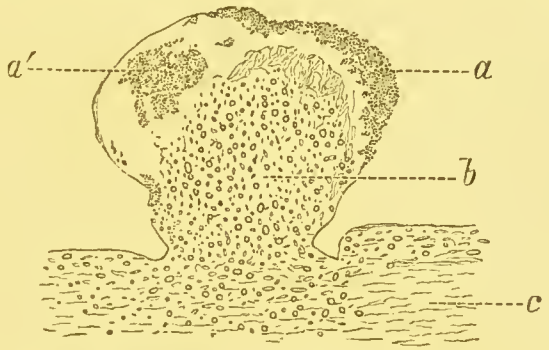

FIG. 8.*—Mycosis Endocardii. Minute vegetation on mitral valve. (*a*) Colonies of micrococci aggregated on surface of vegetation. (*a'*) The same embedded in the semi-translucent (fibrinous) portion of vegetation. (*b*) The granulomatous basis of the vegetation. (*c*) Superficial layers of endocardium infiltrated with leucocytes.

manifested upon valves already diseased. The acute is grafted upon the chronic condition.

It must be taken as proven that micrococci are constant elements in ulcerative (malignant) endocarditis. Dr. Osler says: "They vary a good deal in number and arrangement, and may be scattered singly in the granular substance or arranged in groups. They are usually very numerous at the deepest part of the vegetations, just where the structureless material joins the granulation-tissue, and they may penetrate deeply into the substance of

* From specimen prepared by Mr. G. C. Karop, according to Gram's method.

the valve. Sometimes the smaller vegetations seem made up exclusively of them. Several of my specimens appear to confirm the view of Klebs (*Archiv für Experiment-Pathol.*, Bd. vi.), that the micrococci lodge first in the endocardium and penetrate into the substance, often as distinct columns. In their immediate vicinity there is a zone of necrosis, and beyond this an accumulation of leucocytes and signs of reactive inflammation." (Gulstonian Lectures on Malignant Endocarditis, *British Medical Journal*, March 7, 1885, p. 468.)

The micro-organisms met with in the lesions of ulcerative endocarditis are not always of the same variety. Usually they are minute spherules (micrococci, Fig. 7); but small rods (bacilli) have been observed. In cases complicated with tubercle, the bacillus tuberculosis has been found in the diseased portions of endocardium (cf. Cornil, *L'Abeille Médicale*, No. 51, 1884; Kundrat, *Semaine Médicale*, 25 Fev. 1885, p. 66).

M. Jaccoud* has met with three forms: (1) one lanceolate, ovoid and encapsuled, analogous to the microbe found in pneumonia; this form existed in three of his cases; (2) a second, spherical, occurring in groups or linear series like the micrococci met with under conditions of suppuration; such was observed in four cases; (3) an elliptic micrococcus larger than the others, described by M. Netter Prof. Jaccoud's aide-de-clinique. The micrococci have been found not only in the lesions post-mortem, but in the blood of the patient withdrawn during life. In a case

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* "Endocardite Infectieuse": *La Semaine Médicale*, 24 Fev. 1886, p. 70.

recorded, Prof. Jaccoud says: "The blood showed a notable quantity of micro-organisms, rounded, mobile, isolated or united in couples or in chains to the number of five in each chain; the blood was cultivated, the second cultivation showing the same elements." After death, like micrococci were found in a lacerated part of the uterus (the case being one of puerperal endocarditis), in the vegetations upon the mitral valve, and in the pus which was found in the membranes of the brain. (*See* Note A.)

Very important experimental evidence has lately been adduced by Orth of Göttingen, at the Congress of Naturalists and Physicians of Germany, held at Strasburg, 18th to 23rd of September, 1885, on the question of the precise relation of micro-organisms to the lesions of ulcerative endocarditis. Rosenbach and Orth had previously determined that direct irritation of the valves of the heart of a rabbit did not produce endocarditis. Orth then, in conjunction with Wyssokowitsch of Kharkoff, endeavoured to ascertain whether the injection of any of the various forms of micrococci would induce the disease, but the results were in all instances negative. When, however, the two proceedings were combined—that is, when an artificial lesion of the valves was produced, and immediately or shortly afterwards, liquids containing certain micro-organisms were injected into a vein of the ear, an acute endocarditis was induced which caused the death of the rabbit in from two to five days. The pathological appearances were precisely those of ulcerative endocarditis in the human subject. It may therefore be concluded that ulcerative endocarditis can be produced by the influence of micro-organisms in animals, but only when there is antece-

dently or concurrently a lesion of the endocardium—such lesion may be extremely slight, a mere rubbing with a probe over the surface of the valve being sufficient.*

In the autopsies which I have taken as illustrative, ulceration was observed in six. The ulceration affected the aortic valve in three cases, the mitral in two, and both aortic and mitral in one case. Dr. Osler's records show the following as the relative frequency with which different parts of the endocardium are attacked—Mitral valve alone, 77 cases; aortic valves alone, 53; aortic and mitral together, 41; heart-wall, 33; tricuspid valve, 19; pulmonary valves, 15.

I turn from this brief review of the morbid anatomy of the affection to—

II. *The Rise and Progress of Endocarditis, as evidenced by Clinical Observation.*—The fact which stands out pre-eminently in this connection is the association with rheumatism, acute and subacute. This association has been noticed ever since adequate means have existed for the detection of morbid changes in the valves of the heart; to Bouillaud must be ascribed the merit of first calling prominent attention to it. It is now a matter of common experience with all of us who have to treat cases of rheumatic fever. We know that in any case of this disease there is a strong probability of endocarditis becoming manifest by a change in the valves of the heart. Discrepancies exist as to the proportion in which valvular complications are declared in acute rheumatism, but these are probably susceptible of some

* *Semaine Médicale*, September 23, 1885, p. 319.

explanation. Amongst English observers (Fuller, Sibson, Budd, Latham, and others) the figures approximate tolerably closely, and indicate that in acute rheumatism endocarditis becomes manifest in one out of every two or three cases.* Continental observers, however, record a less proclivity, the figures of Bamberger, Lebert, Wunderlich, and Roth showing a proportion of one in five to eight cases.† The statistics collected for me by Dr. Gabbett and Dr. Coxwell from the records of the London Hospital show as follow:—In 1880, 113 cases of valvular complications were noted in 244 cases of rheumatic fever, a proportion of 46·3 per cent.; in 1881, 170 in 295, or 60·6 per cent.; in 1882, 305 cases of rheumatic fever were admitted; of these 175 exhibited valvular disease, the percentage being 57·3.

The increasing proclivity to valvular complications with repeated attacks of rheumatic fever is shown thus:—In 1880, in cases of a first attack of rheumatic fever valvular changes were evidenced in 44 per cent. In cases admitted for a *second* attack of rheumatic fever the proportion was 48·5 per cent. In those who had suffered from two or more previous attacks the proportion was 59·0 per cent. In 1881, the valvular morbility was in the first attack slightly reduced (viz., 41·8 per cent.), whilst in the second attack it had greatly risen (viz., to 70·8 per cent.), and after two or more attacks stood at about the same ratio (67·1 per cent.) In 1882 valvular changes were noted in 48·1 per cent. of the patients suffering from

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* *Cf.* Hayden, "Diseases of Heart and Aorta," p. 304 *et seq.* Dublin: Fannin. London: Churchill. 1875.

† Rosenstein in "Ziemssen's Cyclopædia," vol. vi. p. 85.

a first attack; in 66·6 per cent. of those suffering from a second attack; and in 77 per cent. of those suffering a third attack and over.

To modify the plan of observation, the heart was *noted as healthy* in 1880, in cases of a first attack of rheumatic fever in 50 per cent., in cases of a second attack 40 per cent., and after two or more attacks 20 per cent. In 1881, the record of "healthy heart" was in the ratio of 37·1, 19, and 22·8 per cent. in the three classes respectively. In 1882 the heart was healthy in 46·8 per cent. of those admitted for a first attack; in 25·2 of those admitted for a second attack; and in 18·7 per cent. of those who had, previously to admission, suffered two or more attacks.

We may now inquire by what signs the advent of endocarditis in the course of acute rheumatism is declared? I exclude those cases which are complicated by pericarditis, because they are out of the scope of my subject. First, as regards *symptoms*. These, according to the experience of many with which my own observations are entirely in accord, are by no means characteristic. Oftentimes there is absolutely no subjective sign which might give rise to the suspicion that the lining membrane of the heart is becoming involved in a serious disease. The course of the rheumatic fever appears to be modified in no appreciable degree. I am aware that some observers have laid greater stress on the prevalence of such subjective signs. The late Dr. Sibson, for instance, stated that in nearly every one of his cases developing heart complications in acute rheumatism the inflammation "pronounced itself by the immediate language of the heart itself, by pain in its region, by the anxious

expression of the face and its dusky or glazed hue, and by the disturbed breathing."*

Next, as to the *physical signs* by which the endocardial implication is indicated or rendered probable. I believe the most frequent sign to be a *prolongation of the first sound of the heart.* Sir William Gull and Dr. Sutton have noted this sign. They say: "Such a prolonged first sound not unfrequently in the course of a few days becomes a well-marked mitral bruit. . . . . It also occasionally happens that the first sound is prolonged at the apex, and continues so until the patient is almost, if not actually, convalescent; and then this prolonged sound becomes a decided mitral murmur."† Dr. Sibson made a similar observation. Prolongation of the first sound was noted by him in eighteen out of twenty-two cases of threatened rheumatic endocarditis.‡ My own view as to the significance of this sign is that it is due to an impairment of the valvular element of the first sound. The curtains of the valve being swollen, the flap of their closure is rendered less manifest; the ear consequently perceives, for the most part, the muscular element of the systolic sound. The period of the disease at which manifestation of the involvement of the endocardium occurs is an important, though a debatable, question. Hayden placed it from the sixth to the ninth day of an attack of acute rheumatism;§ Fuller from the sixth to the twentieth day. Gull and Sutton say, however: "Experience teaches that the heart

* Address in Medicine: *British Medical Journal*, Aug. 13, 1870, p. 161.

† *Medico-Chirurgical Transactions*, 1869, p. 82.

‡ *Loc. cit.*, p. 162.

§ "Diseases of Heart and Aorta," p. 799.

becomes diseased at the very outset of the rheumatic fever, before the patients enter the hospital,"* and Sibson was in accord with this observation: "The prolongation of the first sound, when present, was generally audible on the first day." I consider that though the prolongation or murmurish character of the first sound may be heard at variable periods of the evolution of rheumatic fever, it is very common to find it, as the observers last quoted have said, at the very earliest periods of evolution of the disease. I shall again call attention to the importance of this observation. But even though a distinct mitral murmur be noted this must not be taken as conclusive evidence of disease of the valves, for it may be due to regurgitation from passive yielding of the ventricular muscle. This we shall consider in the lecture on Mitral Regurgitation.

A prolongation of the first sound or the production of a veritable systolic murmur does not, however, constitute the only sign of involvement of the endocardium in disease. To one sign I wish to call particular attention, chiefly because I want more evidence on the point. I have observed, as an early sign, *reduplication of the first or of the second sound* of the heart, and, so far as my experience has gone, when I have observed this sign the resulting change upon the valve has induced, not mitral regurgitation, but mitral stenosis. I have formerly before this Society developed my views as to the manner in which such reduplication, or seeming reduplication, is effected.†

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* *Medico-Chirurgical Transactions, loc. cit.*, p. 80: *British Medical Journal, loc. cit.*, p. 162.

† *Proceedings of the Medical Society of London*, vol. v.

And, again, the change may be noted exceptionally in the aortic and not in the mitral valve. I have observed, during the evolution of rheumatic fever, a musical diastolic murmur becoming manifest at the base of the heart. My view is that such murmur is caused by the vibration of a pedunculated vegetation depending from an aortic cusp.

The next inquiry I would make is, Whether is there any causal relation between the pyrexia of rheumatic fever and the occurrence of endocarditis? Wunderlich says: "Cardiac complications are by no means excluded by the absence of fever."* My own experience is entirely in accord with this statement. Again, cases of rheumatic fever which manifest hyperpyretic temperatures are not accompanied by an abnormal proportion of valvular complications. In fact, the report of the Committee of the Clinical Society on Hyperpyrexia in Acute Rheumatism, states that endocarditis was a little less frequent in such cases than in rheumatic fever generally.† The conclusion, therefore, is irresistible, that there is no relation of causation between pyrexia and endocarditis.

Some authors have considered that there is a relation between the severity of an attack of rheumatism, the extent of the polyarthritis, and the development of valvular disease. I can only say that such is not my experience. This will engage our attention immediately.

Let us now inquire concerning those cases of Endocarditis which are not associated with a history

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* "Medical Thermometry," New Sydenham Society's translation, p. 390.

† *British Medical Journal*, June 3, 1882, p. 807.

of Acute or Subacute Rheumatism. These may conviently, for purposes of investigation, be divided into two classes—(1) those which are observed in early life; (2) those which develop after maturity. In the latter class are those cases of gradual onset which involve the aortic orifice, and sometimes the mitral, which are traceable to subinflammatory changes at the root of the aorta, and degeneration subsequently. In these cases the Endocarditis and Valvulitis are consecutive—they have no necessary connection with rheumatism, and their consideration may be conveniently deferred.

The study of Endocarditis as it occurs in the early periods of life is, however, at the point at which our investigation has hitherto been advanced, a matter of very great importance. Almost every practitioner is familiar with the fact that cases of disease of the valves present themselves which have shown evidence of such disease for many years, from very early periods of the life of the patient; and yet inquiry fails to elicit that the subject of such disease has ever suffered from rheumatism in any form. It is surely a matter of importance, therefore, that we should endeavour to learn how such disease originates in the period of childhood.

I have elsewhere discussed this question at some length,* and I shall here only call your attention to a summary of such points as I think are absolutely necessary to bear in mind when we are considering Endocarditis with a view to treatment. I may, however, cite some evidence supplementary to my former

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* Clinical Lectures on Diseases of the Heart in Children: *Medical Times and Gazette*, 1879.

lectures, derived from a summary of more recent cases prepared for me by Mr. J. A. West, our House-Surgeon, and formerly our Registrar, at the North-Eastern Hospital for Children.

In acute and subacute rheumatism in the child, it has been considered by West, Rilliet, Barthez, and others that the proneness to Endocarditis is greater than in the adult. Rosenstein * has combated this view; but he considers "the disposition to endocardial affections on the whole less in childhood than after puberty." My experience entirely coincides with that of Dr. West, and is against Rosenstein, whose only recorded argument is that "he has repeatedly seen cases of rheumatic arthritis, even in children, which were not followed by endocarditis." Typical rheumatic fever is much less common in the child than in the adult; the articular manifestations are slighter, but I consider the morbility of the endocardium to be greater. Of thirty-two cases of acute and subacute rheumatism occurring in children under twelve years of age admitted into the North-Eastern Hospital during three years, twenty, or 62 per cent., presented signs of endocardial affection. The development of endocarditis, however, in the child has not so close a relation with the other phenomena of rheumatic fever as in the aduit. It may precede, or may succeed, even after long periods, the attack. We meet with cases of Endocarditis in children by no means uncommonly where the manifestations of rheumatism are very slight. There may be no history of subacute rheumatism, but only very slight pains, often designated "growing pains." Valvular complications

* "Ziemssen's Cyclopædia," vol. vi. p. 85.

have been noted by me in the following proportions in the three classes of cases: (*a*) acute rheumatism, forty-seven cases; (*b*) subacute rheumatism, twenty-one cases; (*c*) rheumatoid pain, eight cases.

Again, the manifestation, or, rather, indication, of rheumatism may be even slighter still. I have noted Endocarditis in cases where *eruptions* have been the only indication (if so they be admitted) of the rheumatic diathesis. Such eruptions are *eczema*, *erythema* (*e. circinatum* or *e. marginatum*), and *purpura*.*

But there are other diseases besides rheumatism in the child with which Endocarditis stands in close relation. These are chiefly Scarlatina and Measles. In relation with Scarlatina, Endocarditis may occur either with or without the intervention of articular symptoms. Post-scarlatinal rheumatism is well known, and bears a close similarity to ordinary rheumatic fever; associated Endocarditis is therefore rendered probable. But I have shown from recorded cases that such Endocarditis may become manifest after Scarlatina, not only without the intervention of articular phenomena, but long after the period of fever has passed, and during a time when there is no elevation of the temperature of the body, no pyrexia whatever.†

Again, there is evident proof that Endocarditis can arise in close relation with *Measles*. I have recorded a case in which both Pericarditis and Endocarditis occurred a fortnight after the commencement of con-

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* *Vide* Lectures on Diseases of the Heart in Children: *Medical Times and Gazette*, Dec. 27, 1879, p. 711.

† *Ibid.*, Oct. 25, 1879, p. 472.

valescence from Measles. At this time a perilous attack of Chorea developed. There was in this case no obvious manifestation of Rheumatism, nor hereditary tendency thereto. It appears to me that the influence of Measles in predisposing to Endocarditis has been much under-rated. And, *à fortiori*, the frequent sequence of these diseases, as observed in children, becomes an agency, as I think very probable, not only to the production of the endocardial disease, but to acute rheumatism itself. To take examples—

1. Scarlet fever, measles, and subacute rheumatism in one year; mitral regurgitation.

2. Scarlet fever at age of two; second attack at eight, followed by measles and rheumatoid pains; mitral regurgitation.

3. Measles at age of two, scarlet fever at three; mitral regurgitation and aortic obstruction.

Of nine other cases in which measles was noted in the previous history of cases manifesting endocardial murmurs, acute and subacute rheumatism were manifested in four.

After measles, just as after scarlatina, Endocarditis, or Pericarditis, or both combined, may develop, with no signs of pyrexia.

Excluding all these probable causes, however, there yet remains a very considerable minority of cases of Endocarditis in children in whom no traceable disease has led up to the valve-deterioration. The condition is only betrayed by various morbid conditions, the results or concomitants of the valvular disease. I have noted twenty-seven of such cases. They have been marked by (*a*) disorders of the nervous system —hemiplegia, hemianæsthesia, epilepsy, chorea; (*b*) disorders of nutrition—wasting, anæmia, &c.; (*c*) dis-

orders of respiration or circulation—cough, dyspnœa, or the usual phenomena of progressive cardiac failure.

This evidence proves, I think, that in the child endocarditis can arise and progress without special symptoms, without pyrexia, without the disturbing influence of any acute disease. It may be asked, however, whether the form of endocarditis in such cases differs in any way from that which we know as the rheumatic form. The answer is given by the post-mortem evidence. There is no obvious difference from the essential features of rheumatic endocarditis, such as we find in the undoubtedly rheumatic subjects.

Such is the evidence—the important evidence, as I estimate it—to be obtained as to the rise and progress of Endocarditis from the clinical observation of the cases occurring in children. It becomes us, however, to revert to the general subject, to the disease as it is seen in adults, and to inquire whether there are any other diseases with which we find endocarditis associated. In many acute fevers, *typhoid* for example, it is so rare that I consider it most probable that some other factor must have been in existence in the cases in which it has been observed. In *diphtheria* endocarditis is so infrequent that it cannot be contended that any causal relation exists between the two diseases.

An association between *Septicæmia* and Endocarditis is undoubted. The origin of such septicæmia may be traumatic or puerperal, and the endocarditis is of the ulcerative form. Kundrat has adduced a case in which a workman after a slight burn suffered from lymphangitis and malignant endocarditis, and micro-

organisms were found in the lesions. In another case ulcerative endocarditis supervened upon a wound of the uterus made in an attempt to procure abortion. Very slight injuries, such as paring a hang-nail or a corn, or the passage of a sound through a stricture, have been the precursors of endocarditis of the ulcerative form. In the puerperal category we may recognise cases which (*a*) occur during pregnancy, with no obvious determining cause; (*b*) after abortion, with a course not essentially differing from that of uncomplicated septicæmia; (*c*) after normal parturition.

Another association of Endocarditis (still of the ulcerative form) is with *acute osteo-myelitis*. A case is cited by Dr. Osler of a lad of ten in whom there was ulcerative endocarditis of the right side of the heart, with a purulent focus in the septum: "It was only after most careful search that the primary trouble was found in a small spot of acute necrosis of the tibia."* The interest of this observation is greatly increased owing to the recent observations on the nature of the disease known as acute osteo-myelitis, communicated by M. Socin of Basle to the French Surgical Congress, 7th April 1885. M. Pasteur had long ago described a spherical micro-organism as present in the pus both of acute necrosis of bone and of ordinary phlegmon. Rosenbach (of Göttingen), and Krause (of Halle), found in the two affections equally two distinct varieties of micrococcus, the one yellow (*Staphylococcus pyogenes aureus*), the other white (*Staphylococcus pyogenes albus*). To these Rosenbach

* Gulstonian Lectures: *British Medical Journal*, March 14, 1885, p. 522.

subsequently added a third, which consisted of more minute spherules united in chains and not in masses as the former. This variety was termed *Streptococcus pyogenes* (Fig. 9). M. Garri, deputed by M. Socin, examined thirty cases of acute osteo-myelitis with the result of confirming the former observations, the varieties of micrococci above mentioned being invariably discovered in the purulent infiltrations. Further observations were made in cases of abscesses, phlegmons, &c., with the result that out of seventy-six cases the staphylococcus alone was found in sixty-

A. B.

FIG. 9.—A, *Staphylococcus pyogenes aureus* and *albus*. These are indistinguishable except by cultivation, the one producing golden-yellow, the other opaque white colonies. B, *Streptococcus pyogenes*.

eight cases, the streptococcus alone in six, and the two forms combined in two cases. It would appear from these observations that the same causes which induce osteo-myelitis can also induce other affections in which suppuration is a marked feature, and that these causes exist in the form of certain micro-organisms. To further elucidate the question, M. Garri determined to practise inoculation upon himself of the microbes obtained by artificial cultivations. A small inoculation in the neighbourhood of the finger-

nail gave rise to a distinct abscess, and the pus from this abscess inoculated upon gelatine reproduced pure cultivations of the *Staphylococcus aureus*, cultivations which manifested their special characters for many generations. Lastly, M. Garri rubbed into the skin of his left arm a solution containing a cultivation of the microbe obtained from osteo-myelitic pus. The result was the rapid development of a severe inflammation, with necrosis of tissue, extensive suppuration, and grave constitutional disturbance. The dangerous experiment issued in recovery, but seventeen cicatrices bear witness to the morbific agency of the micrococci. It was the same micro-organism, the staphylococcus, which, when injected into the circulation at the same time that a traumatic lesion of the valves was in existence, was associated with the production of ulcerative endocarditis in Orth's experiments. A like result attended the injection of cultivations of the streptococcus, which appears to be even more virulent than the former. On the other hand, the injections of some other forms (*Micrococcus tetragonus*, the *Pneumococcus* of Friedländer, &c.) were not associated with any ulceration of the endocardium.

Ague has been found to be associated with Endocarditis both of the simple and of the ulcerative form, and cases have been recorded by Lancereaux, Greenhow and others, but the evidence is insufficient for any generalization. Endocarditis has also some association with pneumonia. Dr. Osler found in 103 autopsies of cases of lobar pneumonia, evidences of acute endocarditis in sixteen; eleven being of the ulcerative form. In the majority of cases, Dr. Osler says, there is a history of ordinary pneumonia having its usual

course; then a day or two after defervescence, fever of an irregular type recurs, and typhoid or pyæmic symptoms arise. In some cases rheumatic symptoms are manifested. The etiological relation between the pneumonia and the endocarditis is yet obscure, but evidence is accumulating in support of the proposition that many of the forms of pneumonia are infective and associated with micro-organisms.

In considering the general question of the *Pathogenesis of Endocarditis*, we may review the cases under three classes—first, those associated with rheumatism; secondly, those associated with diseases and conditions of infection; thirdly, those manifesting a malignant course and attended with ulceration, in which there is association with no morbid agency as yet discovered. We exclude for the present those cases of atheromatous change with which chronic changes in the endocardium may be associated, and on which ulceration not having the characters of the malignant form may be engrafted.

First, the *rheumatic form* of Endocarditis, which includes the cases manifesting the simply exudative and the sclerous forms that I have described, the sclerous being the chronic form of the exudative. Clinical experience has taught us that such endocarditis may arise in an extremely insidious manner, that it may give no evidence of its onset and progress by signs nor symptoms, nor even by rise of temperature. It may probably be in existence at the very earliest period of an attack of rheumatic fever, and even with great probability precede it unnoticed (for such may be the significance of the muffled or prolonged first sound heard at the earliest period of such disease). Moreover, it may progress after the attack

of rheumatic fever, causing gradual induration or retraction of the valve in a patient who may have been discharged from treatment as free from cardiac complication. Such is the disease—insidious in onset, course, and character—the causes of which we have to consider.

However occult its origin and course, we must allow that the inflammation of the endocardium is an integral part of the rheumatic process, that it is produced by the same agency which in many cases, though not in all, produces inflammation of the fibrous textures of the joints. Such morbid agent is, without doubt, distributed by the blood. The question occurs, Is it introduced from without or developed within? The view of its extrinsic nature has been forcibly argued by Dr. Maclagan.* The hypothesis is that the *materies morbi* which produces it is a form of malaria, and, as such, of the nature of a micro-organism. There is no direct evidence to support this view. It must be agreed that ordinary endocarditis, though often associated with a form of rheumatism manifesting pyrexia, is not essentially a pyrexial disease. A wave of inflammation involving the endocardium and valves, and even the pericardium in considerable intensity, can be manifested without any ascertainable modification of the ordinary temperature of the body. Moreover, except in the case of ulcerative endocarditis which we have yet to consider, no association with micro-organisms has been demonstrated. It is true that Klebs discovered micrococci in the warty outgrowths, but Orth says

* "Rheumatism: its Nature, its Pathology, its Successful Treatment." London: Pickering & Co. 1881.

that he could find none in the vegetations of simple endocarditis and cultivation-experiments in two cases were without result. It is probable that the vegetations examined by Klebs covered actual ulcerations of the endocardium. It may justly be objected that the non-existence of pyrexia is by no means fatal to the view that endocarditis is due to the operation of micro-organisms, and the example of syphilis may be cited. Indeed, the fibrous, sclerous tracts of endocardial thickening may be said to resemble the results produced by syphilis on mucous membranes and on some fibrous structures; but it must be remembered that there is in case of rheumatic endocarditis a total negation of the possibility of transmission from person to person.

The older hypothesis is that the endocarditis as well as the other phenomena of rheumatism are due to a perverted retrograde metamorphosis. The evidence to this effect, though not conclusive, is cogent. First we have hereditary proclivity. This, I consider, obtains both as regards rheumatism in general and endocarditis in particular. Then, in regard to proximate cause. Some cases can be distinctly traced to a sudden exposure to cold—immersion in cold water, for instance. Others are in association with diseases which impede elimination by the skin, by the kidneys, or by both channels. In the next place we may note the proved conditions of the disease. An extremely acid sweat is thrown off; lactic acid has been demonstrated as a constituent thereof, but it is not proved that lactic acid is the only compound excreted. Certainly there must be some other agent to communicate the peculiar odour which the perspiration manifests. Again, the urine is abnormally acid. And the saliva,

which is normally alkaline, is, in rheumatic conditions, decidedly acid. Furthermore, the blood is abnormal in that it contains an undue proportion of an excrementitious product—viz., fibrin; it is highly coagulable. M. Hayem (Société Médicale des Hôpitaux de Paris, January 22, 1886) has recently contended that the diagnosis of rheumatism, even before its ordinary phenomena have begun to be manifested, may be made by the examination of a drop of the blood of the patient, a strong reticulum of fibrin being observed. Though there is abundant evidence to prove that in rheumatism an acid is eliminated, it is shown that the blood itself is not acid but alkaline.

Hence, though we cannot point to a definite chemical body as the agent in the production of rheumatism and its attendant endocarditis, we have full and sufficient proof that the normal retro grade metamorphosis is greatly altered; that the blood is changed; that in the course of metabolism many products are formed, with the result that lactic and other acids are excreted in abundance. Sufficient, this, I think, for our present purpose. Is it not probable that the pathogenetic agents are many —I mean, that there are numerous products of the disturbed metamorphosis capable of giving the irritating impulse?

One step further in this inquiry. The *rôle* of the nervous system in this connection may be a very important one, and we may ask whether there may not be a portion of the central nervous system specially concerned in the control of the chemical processes of metabolism, just as there is probably a centre which regulates the temperature of the body. Dr. P. W. Latham has advanced the theory that there is such a

centre—that this may be disturbed by external cold or by the accumulation of lactic acid in the blood. So he considers that the phenomena of rheumatism may be induced by an intra-spinal change just as the arthropathies are induced in locomotor ataxy. And if the disturbance of such centre involve also the neighbourhood of origin of the vagus, cardiac, pulmonary, or pleuritic complications may be developed.*

When a muscle contracts, and when it ceases to live, there occurs a rearrangement of its molecules—lactic acid and carbonic acid are formed—that is to say, "the molecules forming these substances are detached from the muscular tissue." Dr. Latham says: "I would suggest that the change in the molecular constituents of the muscular tissue which leads to the further development of heat, results from a weakening or lessening of the power, whatever that may be, which holds the molecules together; that with the dilatation of the vessels in the part, under the influence of the vaso-motor nerves, there is also a splitting-up or tumbling to pieces of the albuminoid molecules, and from both causes heat is developed. The normal change of the cyanalcohols is interfered with. Their condensation into higher cyanalcohols with elimination of urea, or their change into cyanamides and amido-acids with the ultimate oxidation of the latter, is modified. The molecules $CH_2 \left\{ \begin{matrix} OH \\ CN \end{matrix} \right.$ and $C_2H_4 \left\{ \begin{matrix} OH \\ CN \end{matrix} \right.$ become detached more or less from each other, and by

* Some Points in the Pathology and Treatment of Acute Rheumatism and Diabetes: *Lancet*, Jan. 8, 1881; and *British Medical Journal*, Jan. 14, 1882.

hydration (by which heat is developed) form substances—glycollic acid and lactic acid—which are oxidized more readily than the amido-acid glycocine which is also formed. The oxygen, though conveyed in larger quantities than normal by the increased blood-supply to the tissue, is completely used up in oxidizing into carbonic acid and water the glycollic and lactic acids which have been formed; the excess of lactic acid and the glycocine are unoxidized, and pass into the circulation." *

We have now to consider the question of the pathogenesis of the endocarditis which is in association with known infective diseases. In this connection we have, in the first place, Scarlatina and Measles. In neither instance have we evidence that the *materies morbi* of these diseases is the *direct* cause—in neither does the endocarditis develop in strict relation with the initial fever; in fact, it is rather in the relation of an *epiphenomenon*. In scarlatina there is a distinct impediment to elimination by the suppression of the functions of the skin and the kidneys, and the endocarditis as well as the rheumatic symptoms which develop may be due, as in the uncomplicated cases of rheumatism, to a disturbance of metabolism. The interference with the normal functional activity of the skin and the mucous surfaces in measles may bring about a like result, and so superinduce the endocarditis which arises in association with some cases of this disease. Whilst considering it more probable that the germs of infectious disease stand in the

* Croonian Lectures on some Points in the Pathology of Rheumatism, Gout, and Diabetes, delivered at the Royal College of Physicians, by P. W. Latham, M.D., F.R.C.P.: *Lancet*, April 17, 1886, p. 676.

relation of a remote rather than a direct cause, I am by no means reluctant to admit the probability that so-called rheumatic fever may in many instances itself be the outcome of a previous infection, often perhaps undetected. Many observers have recorded instances in which sore throat, unattended with the signs of scarlatina, has been followed by well-defined articular inflammation of the nature of acute rheumatism.* I have myself observed some instances. Dr. Stewart † says that in many such cases the throat affection may be unnoticed by the subject, and its very existence may be altogether overlooked unless the physician examine the throat in every case. My observations entirely confirm this. Many patients who have denied that they have ever been subjects of sore throat, have manifested on examination such losses of substance in the tonsils, or such cicatricial changes, as to prove with certainty that an ulceration had occurred at some period of their life-history.

The following case seems to me instructive in reference to this question:—

Mary Jane R., a servant, aged twenty-four, was admitted under my care into the London Hospital, November 30, 1882. She suffered from pains in most of the joints, with profuse perspiration; in fact, manifested the signs of acute rheumatism. Five years previously she had an attack of acute rheumatism, with subacute signs occasionally since. On this occasion the illness had commenced with sore throat

* *Cf.* On Rheumarthritis, Carditis, and Chorea, with a new Theory of their Unity of Origin, by William Stewart, F.R.C.P.E., Honorary Surgeon to the Beckett Hospital, Barnsley: *British Medical Journal*, Nov. 11, 1882, p. 940.

† *Loc cit.*

and lumbar pain. Very soon after admission the pain became exceedingly acute, preventing the slightest movement: then she became semi-comatose. The urine passed the first day was only half an ounce in quantity, and contained blood and renal epithelium. She made no complaint of sore throat, but on my examination I found a well-marked ulcer of the tonsils commencing to cicatrize. She was treated by hypodermic injection of pilocarpin (gr. $\frac{1}{6}$), followed by hot-air bath and administration of diuretics. The daily excretion of urine was in ounces successively—16 ounces, 8, 24, 38, 40, 50, 30, 20, 25. Albumen ceased to be discovered after the eighteenth day. The arthritic pains gradually decreased until complete recovery. The saliva gave a very acid reaction for six weeks, and then became much less acid.

In this case the first aspect was that of ordinary rheumatic fever, occurring in a patient who had previously suffered from the same affection; it was soon seen that a condition of anuria with acute nephritis differentiated it from ordinary rheumatism. The condition of the throat at once showed that an ulcerated tonsillitis of septic character was in existence, and accounted with great probability for the renal inadequacy and the determination of the rheumatic phenomena.

Endocarditis when occurring in coexistence with infection from post-partum lesions or from traumatic agencies, looks at first sight as if it were in the direct relation of effect from causes derived from without. These points, however, have to be taken into consideration: (1) that the acute and special morbid action is manifested in the majority of cases

not upon healthy endocardium, but on endocardium already diseased; (2) that the septic diseases above mentioned are often associated with an arthritis and with other symptoms closely resembling, or identical with, acute rheumatism. So in these cases also it is probable that the phenomena of rheumatism and of endocarditis are epiphenomenal, and due to the perversion of metabolism occasioned by the septic lesion; the specific micro-organisms not determining the endocarditis but modifying it, entering and destroying the already diseased endocardium and causing the ulceration and destruction rather than the initial inflammation. To the experimental evidence in favour of this view, I have already alluded.

Endocarditis, however, of the maligant character may occur in association with none of the causes which I have mentioned. It may seem to be idiopathic. In these cases (I use Dr. Osler's words) "the disease may set in with a single rigor or a series of chills, most frequently the former; often a period of *malaise* or ill health has preceded the attack, and in very many instances the symptoms develop in the course of some fever. The characters of this form are irregular temperature, early prostration, and involvement of the nervous system, delirium, somnolence and coma, dry tongue, relaxed bowels, sweats, petechial and other rashes, and occasional parotiditis. Perhaps the majority of cases are mistaken for typhoid, as the heart symptoms may never be prominent, or even when sought for not found." * It is scarcely possible to conceive other-

* Gulstonian Lectures, by Dr. Osler: *British Medical Journal*, March 14, 1885, p. 523.

wise than that this *ensemble* is the outcome of the operation of some septic agency or agencies; and in the lesions of the endocardium found on post-mortem examination, micrococci are invariably present. In some cases the endocardial involvement is very slight, as in a case of Dr. Osler's, when its only lesion was "mitral valves a trifle thick, with small superficial losses of substance on both curtains." In others there are vegetations of the most pronounced character, and abundant erosions of the endocardium. The evidence obtained from investigation of this form of endocarditis would not permit us to deny that the occult and undiscovered septic agencies *might* be directly destructive upon the previously healthy endocardium, but the analogies would rather point to the conclusion that this follows the same laws as the septicæmic forms, wherein the source of the *materies morbi* is traceable to the decomposing surface of a wound in direct contact with the air. In the untraced or so-called idiopathic form the pathogenetic germs enter the body by channels which are unknown, but once entered they operate most probably in a like manner with those which are more amenable to investigation—that is, they produce endocarditis indirectly by their interference with tissue changes and ulceration by the direct agency of the living *materies morbi*. It does not seem to me impossible that the necrotic process may be started by mere violence done to the valves. The sequence may be as follows:—The absorption of *materies morbi*, its effect upon nervous centres and heart-mechanism; a violent and desultory action of the latter; such irregular and forcible tension and friction of the edges of the mitral curtains that a slight

lesion of surface is induced; then the entry of micrococci to do their work of destruction.

I now proceed to inquire concerning the efficacy of extant therapeutic methods in regard to rheumatic endocarditis. It has been claimed of almost all the modes of treatment of rheumatism which have been advocated that they have been instrumental in controlling or preventing the cardiac complications of the disease. The individual experience of observers has been cited again and again to point the efficacy of this or that remedy or method in mitigating the chief danger of rheumatic fever. Yet proof of such vaunted efficacy has soon been found to be unsatisfactory, and it may be confidently asserted that no antidotal treatment is yet known—that we have, for instance, no drug which can influence endocarditis as quinine influences ague, or as mercury and iodide of potassium influence syphilis. The discussion, so ably sustained in this Society during a former session, which has been fully reported, has put the claims of various forms of treatment of rheumatic fever to a numerical test.

The results of treatment by rest and mint-water, by alkalies, by blistering, and by administration of salicin and its compounds, were compared, and it is fair to assume that if any agent other than these had been efficient in the treatment of rheumatic fever or of endocarditis, evidence would have made this apparent. The outcome of the discussion, which it is unnecessary to epitomise,* was to show a strong concurrence of testimony to the effect that the

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* Vide *Proceedings of the Medical Society of London*, vol. vi.

administration of salicin or the salicylates decidedly reduced the suffering and the fever of rheumatism, but in no marked degree influenced the development of endocarditis and other cardiac complications. *Primâ facie* this seems to be a strange conclusion, for one might imagine that an agent that subdued so decidedly the pain and fever which must contribute to disturb the heart, even if it had no pronounced effect upon the rheumatic process within the heart, would, with great probability, influence for good the inflammatory process in pericardium as well as endocardium. The conclusion is forced home, however, alike by individual experience—for pericarditis and endocarditis are shown by physical signs to arise and progress in patients who are fully under the salicin treatment—and by statistical inquiry from large numbers of cases treated by the salicin compounds compared with those treated in the pre-salicylic era, such as has been carefully followed out by Dr. Gilbart Smith.* Dr. Maclagan, to whom the profession and the public are indebted for the introduction of agents which have, at any rate, been proved to contribute to the comfort of suffering patients, himself allows that the hopes that they would ward off cardiac complications have not been realized.† He considers the reasons for such failure to be—(1) that endocarditis has often begun in an attack of rheumatism before the sufferings of the patient have been so pronounced as to call for treatment; (2) the inflamed endocardium can never, from the incessant motion of the heart, be placed in the

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* *Lancet*, Jan. 28, 1882, p. 135.

† "Rheumatism," p. 266. Pickering.

conditions of rest which are necessary for cure. I endorse both these propositions, and will add to them.

To put the matter clinically or practically. We observe, let us assume, a patient in a first attack of rheumatic fever. He presents (A) a murmur indicating an endocardial complication. I think I must have convinced you that such endocarditis may have arisen not during the attack from which he is at present suffering, but from the disease acquired insidiously at some time previously. It is obvious that any remedy would fail to influence the cardiac complication in such a class of cases. Or, (B) a modification of sounds or actual systolic murmur developing at the apex makes us suspect the present rise and progress of endocardial inflammation. But such may have had its commencement long before the advent of the other symptoms, for no sign will betray the gradual swelling of a valve. A swollen valve is not necessarily incompetent. On the other hand, a veritable systolic murmur at the apex is no conclusive proof of endocarditis, for it may be due to adynamia of cardiac muscle. Here, then, is a double source of fallacy in the statistics of the cardiac complications of rheumatism. Or, (C) the patient manifesting no evidence of valvular impairment is at the termination of his attack of rheumatic fever discharged as free from cardiac trouble. Sir W. Gull and Dr. Sutton have said that "if the patients pass the first few days of the rheumatic fever without the heart becoming involved, then they do not contract heart disease during the later part of the rheumatic attack."* Is such a conclusion justified? I think not. A valve

* *Medico-Chirurgical Transactions*, vol. lii. p. 80.

may be inflamed and give no evidence of incompetence; the patient may be discharged and show no signs of cardiac trouble, but a slow process of shrinking or sclerosis may be going on, and when the patient next presents himself there may be undoubted evidence of endocardial mischief. This is, I consider, by no means of infrequent occurrence, and is one reason why a second attack of rheumatic fever is attended with such notable numerical evidence of an increase of cardiac complications.

For such reasons as these I think it impossible, the sources of error being so numerous, that we can get from statistical inquiry satisfactory evidence as to the efficacy of different plans of treatment in warding off endocardial disease, and I dissent from those who hold that a remedy which is efficacious in the treatment of acute rheumatism ought to show, on numerical inquiry, a favourable influence on the correlated heart disease. I consider the treatment by salicin and the salicylates, even though no good results are manifest as regards cardiac complications, to be the most favourable to the patient of all forms of treatment hitherto known.

In such case it may be legitimately asked whether I adopt an altogether pessimist view of the treatment of Endocarditis. Can nothing be done? My answer is—Much, but it must be in the direction of *preventive treatment*.

My own experience is strongly towards the conclusion that Endocarditis is more prevalent, as well as more extensive and severe, among the poor than among the well-to-do. This question is one that might with advantage be put to the numerical test; we greatly want the evidence of the family practi-

tioner to compare with that afforded by our hospital statistics. The predisposing causes to the advent of Endocarditis, which, as I have shown, can arise without the intervention of obviously rheumatic phenomena, are most probably—(1) exposure to vicissitudes of temperature; (2) an irregular and improper dietary; (3) subjection to a zymotic influence—heriditary proclivity to rheumatism in its various manifestations in all cases playing an important part. These are the impulses to a perverted nutrition, resulting in the retention within the blood of those excrementitious products which we may call "the rheumatic poison." Attention to the clothing and proper feeding of infants and children constitutes, in my mind, therefore, the treatment of first importance as regards Endocarditis. There is no need nowadays to insist on the value of preventive treatment as regards the zymotic diseases. This is well recognised. Is it not quite as important as regards the subtle disease we are considering? I would, whilst recognising the difficulties of such proceeding, strongly recommend the periodic medical examination of children, even though they present no obvious signs of disease.

Of no less importance is the treatment in regard to the zymotic diseases which are correlated with Endocarditis—viz., Scarlatina and Measles. The subject of an attack of Scarlatina should be watched with great care for long periods after convalescence. Moreover, the slightest sign of throat-ailment, especially with children, should be looked upon with suspicion. I have no doubt whatever that in a large number of instances ulcerative tonsillitis of zymotic type occurs in children unnoticed and unknown, and that in

many such a renal complication is instituted which is also neglected. The rise of Endocarditis in such a case is, as I have said, not during the period of fever. I do not recognise the influence of morbid germs in *directly* occasioning the inflammatory change in the valves; but subsequently, such may be developed even after long periods. The teaching I would enforce, therefore, is that the subject of Scarlatina or of the allied forms of throat-affection should be watched, protected, dieted, and treated for periods much longer than is now usual. There is, unfortunately, a widely spread tendency to regard measles as a very slight ailment that requires little or no treatment. Experience teaches, however, that it is not only the immediate precursor of broncho-pneumonia frequently, and heart disease occasionally, but that it effects a deleterious change upon the powers of nutrition, which lasts, as in the case of Scarlatina, for long periods. The subsequent treatment, therefore, of the subjects of Measles should, in my opinion, be much more protracted than it is at present.

Such is an outline of what I consider the common-sense treatment of the first causes of Endocarditis. During its rise and progress in an attack of rheumatism, I prefer the treatment by salicin or the salicylate of soda in sufficient doses (usually gr. xx. every two, three, or four hours, till subsidence of the pain and pyrexia, and afterwards the same dose thrice or twice a day). From the evidence of Dr. Isambard Owen there is a good case in favour of combining with this the administration of full doses of alkalies. Vesication by application of liq. vesicatorius in the left axilla I think also of service.

Dr. Maclagan believes that in some cases of endo-

carditis, when myocarditis is an accompaniment, occurring during an attack of rheumatic fever, the salicylates increase the patient's danger. I have already enunciated the view that the obvious lesions of the endocardium are generally accompanied by inflammatory exudation into neighbouring tissues, and I am quite of Dr. Maclagan's opinion that the muscular substance of the heart is involved more frequently than has been generally supposed. The signs indicating that such involvement is considerable I take to be, prostration and anxiety in disproportion to the physical signs, a very marked loss of tension in the pulse, so that the sphygmograph indicates full dicrotism or hyperdicrotism, irregularity of rhythm and a condition of mental hebetude or subdelirium. In such cases the salicylates should be immediately withheld. The reason is obvious, for it is well ascertained that salicylic acid has a depressing influence upon the heart.

In some cases of endocarditis periodic attacks of shivering or erratic elevations of temperature occur, and the fear is present to the physician that a malignant form of the affection may be in course of development. In such, quinine in sufficient doses is often very beneficial. Fränkel * has administered in such instances with success $7\frac{1}{2}$ to 15 grains of quinine sulphate once or twice daily.

I have myself frequently thus administered quinine when the salicylates have been withheld, and when there has been evidence of continuing endocarditis after the subsidence of the pains and the pyrexia of acute rheumatism. It is better, in my

* *Charité Annalen*, tom. viii. p. 273.

opinion, to give one dose of ten grains daily than to administer repeated doses; after administration for four or five days it should be withheld for a day, for it must not be forgotten that quinine has some depressing influence upon the circulation.

It may be asked whether in cases manifesting very low arterial tension and signs of a feeble heart digitalis may be employed whilst endocarditis is still in progress. It would seem *primâ facie* reasonable to administer an agent proved to increase the energy of ventricular contraction, but in practice I have found that the administration is attended with no advantage, and even with danger. Many of these cases are accompanied by pyrexia, and the important researches of Drs. Lauder Brunton and Cash have shown that the vagus centre and the vagus nerve-supply to the heart are so weakened by the effect of heat that digitalis, and probably all drugs which resemble it in action, fail to exert their slowing effect upon the ventricles.* It is very probable that the remedial action which is thus prevented by heat is prevented also by the inflammatory exudation in myocarditis, even though there be no rise of general temperature.

It now only remains for me to allude to the clinical significance of *ulcerative endocarditis* with regard to indications for treatment.

The extant evidence is sufficient to indicate the extreme importance of preserving from zymotic influences those who are the subjects of chronic disease of the

* "Textbook of Pharmacology and Therapeutics," by T. Lauder Brunton, M.D., D.Sc., F.R.S., p. 917. London: Macmillan & Co. 1885.

valves of the heart, and also of treating with extraordinary care any chance suppuration which may occur in any part of their economy.

If in the course of the clinical observation of the subjects of chronic valvular disease some of the following conditions are manifested, there is a high degree of probability that ulcerative endocarditis has been engrafted on the old lesion. These conditions are: (*a*) very marked disturbances of the temperature of the body. It must be distinctly understood that this is not an invariable sign in ulcerative endocarditis. In a case under my care at the London Hospital there was no marked pyrexia whatever, the temperature never exceeding 101° Fahr., and for the most part keeping close to the normal. (*b*) Signs indicative of embolism occurring in arteries of spleen, kidney, brain, retina, &c. In some cases the signs of embolism are manifest in the skin, and valuable aid to diagnosis is thus afforded (*see* Dr. Cayley's case, Medical Society's Proceedings, vol. vii. p. 436; and Dr. Coupland's case, vol. viii. p. 211). (*c*) Cerebral disturbances—*e.g.*, delirium, extreme prostration, symptoms of cerebral or cerebro-spinal meningitis. (*d*) A typhoid state having much resemblance with that occurring in typhoid fever.

When any of these conditions are manifested the case must be looked upon as one of extreme gravity. It has been accepted by many that *ulcerative*, as it has been termed by some observers, or *malignant* endocarditis, as it has been designated by others, is uniformly fatal, and it may be considered a legitimate inference that treatment is of no avail. I venture to demur to both propositions; but first, I am forced to take exception to the terminology—ulcerative endocarditis is a legitimate term from the pathological

standpoint when the necrosing lesions are demonstrated at the autopsy; but I cannot think it thoroughly satisfactory from the clinical standpoint, for it may be impossible in a given case to determine whether ulcerative changes are occurring in the course of endocarditis or no. Again, the term "malignant" is unsatisfactory; for cases presenting malignant aspects *may* recover. I prefer to call these clinical groups, *Grave (or Severe) Endocarditis*, understanding by this term not the usual rheumatic endocarditis, but forms aberrant therefrom, and presenting conditions indicating immediate danger. But to turn from names to facts, I cannot consider it as provedly impossible to arrest the process of necrosis in diseased endocardium which has once begun. The losses of substance in portions of valves and of endocardium found in post-mortem examination of some cases of chronic valvular disease tell of necrosed patches obviously of old date; some of these may be dismissed as insignificant, because they are in structures which have undergone atheromatous change; in others, the ulceration may have been due to mechanical causes, but a few do not seem susceptible of such explanation, and apparently suggest an arrest of an ulcerative process. Some cases, too, have been observed with signs and symptoms impossible to differentiate from those of the so-called malignant type, and yet have recovered. Such cases have been noted by Dr. Stephen Mackenzie and Dr. Gilbart Smith. It would seem not improbable that the reversion to better conditions of nutrition may bring about the death of the micro-organisms which are the agents of destruction, and it is certainly *possible* that the blood may absorb agents which can be fatal to them.

On this latter point the following case, which was under my care at the London Hospital, is instructive :—

Ill-defined and variable cardiac murmurs in a female manifesting extreme adynamia with a peculiar mental condition : evidence of very low arterial tension : auscultatory evidence of progressive endocarditis : no improvement until the administration of thirty-grain doses of sodium sulphocarbolate ; then progressive recovery.—Alice S., aged twenty, was admitted into the London Hospital under my care on Sept. 23, 1885 ; she was poorly nourished, but not obviously anæmic, rather bronzed, but seemed extremely weak and prostrate. She complained of a sensation of weight at the heart and a pain that encircled her at the level of the diaphragm. There was some family history of rheumatism, and the patient herself was said to have suffered from rheumatism with inflammation of the lungs twelve months ago. She stated that she had never been quite well since. There were no signs of other dyscrasiæ. She was a tin-worker, and much exposed to cold air. The illness which made her seek hospital relief commenced about a fortnight previously with sore throat, followed by pain in the head and left side ; for a week before admission she coughed and spat up a little blood. The organs generally showed little abnormality, but breath-sounds were deficient at the base of the left lung, and there was here slight comparative dulness. The outline of the heart as determined by percussion seemed in no way abnormal, there was an indistinct soft systolic murmur at the apex. The urine was of sp. gr. 1020, acid, of amber colour, contained a little mucus, but no albumen. The most noticeable feature

was the peculiar mental condition of the patient—she was fretful and complaining, dozing during the day, but very wakeful at night, asserting that she suffered pain in varying situations, frequently groaning. It was supposed by some that she was hysterical, but it was evident that her condition could not be explained by this term; no pain was produced by pressure over the situation of the ovaries. Ophthalmoscopic examination revealed no abnormalities. The temperature was 101°·4 Fahr.

For seven weeks the patient continued in a very unsatisfactory condition. During this time the following were the chief points noted: (1) the signs on auscultation of the heart varied considerably. The systolic murmur which was at first soft and slightly pronounced, not conducted towards the axilla, became of musical quality, and was heard down the left border of the sternum as well as in its former situation. The second sound heard over the site of the pulmonary valves varied strangely; one day it was slightly pronounced, on another it was accentuated, at another, feebly heard. Just five weeks after admission a short diastolic murmur was heard at the left border of the sternum at the level of the sixth rib; this became more and more marked and was heard at a higher level. It was evident from these signs that endocarditis was progressing. Then (2) observation of the pulse by the finger indicated low tension, but not nearly to such degree as was revealed by the sphygmographic tracing. The trace taken at a pressure of one ounce showed full and hyperdicrotism (Fig. 10); a pressure of two and a half ounces almost extinguished it. I considered this observation to be of very high importance, and I think it also indicates

the value of the sphygmograph in the diagnosis of obscure affections of the circulatory system. It was evident that no ordinary conditions of endocarditis existed. One could understand such an effect upon the radial pulse if there were question of the last stages of a failing heart in valvular disease; but, as I said before, the outline of the heart was normal; if there had been anterior endocarditis it had not been followed by any of the discoverable signs and none of the usual symptoms of advanced valvular disease. I could only come to two hypotheses—either there was extensive myocarditis enfeebling the cardiac fibres, or else a general toxæmia produced the same result in a

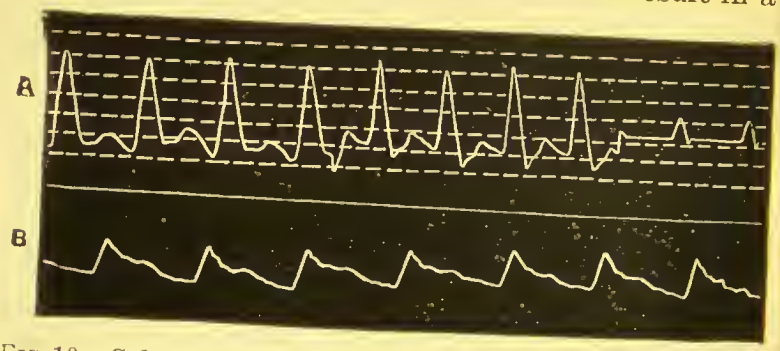

FIG. 10.—Sphygmogram in a case of grave endocarditis. A, Tracing taken during acute period, pressure 1½, 2, and 2½ ounces; B, Tracing taken after recovery.

different way. Then (3) the general condition of the patient, which somewhat resembled that in typhoid—the peculiar hebetude and signs I have noted, constipation alternating with diarrhœa, the continuing prostration, the rapid wasting (the patient lost nine pounds in weight during the first seventeen days, and subsequently lost six pounds in addition), the irregular breathing, the rate of respiration varying, sometimes twenty-eight, sometimes forty-eight. These signs,

taken together with the physical evidences of changing and developing valvular murmurs, led me to conclude that the case was one of severe endocarditis and probably of ulcerative endocarditis. It was true that the temperature did not rise to any considerable height. From 101°·4 it fell to 99° and then did not exceed 100°, for the most part keeping between 99° and 100°. I have found, however, markedly sub-febrile temperature in fatal ulcerative endocarditis proved by post-mortem examination.

And now as to *treatment*. On admission, tincture of perchloride of iron in fifteen-minim doses with twelve minims of tincture of digitalis were administered, the throat, still sore, being gargled with a solution of chlorate of potassium; this plan, with a slight opiate on rare occasions, was continued for thirteen days; then alkalies were administered (ten grains each of the bicarbonates of potassium and sodium), with ten-, afterwards increased to fifteen-minim doses of tincture of digitalis. The case showing no sign of amendment I began, half-heartedly I confess, with twenty-grain doses of sulphocarbolate of sodium, but this was only continued three days and digitalis recommenced. Still no improvement followed, and four weeks after admission I ordered quinine sulphate in five-grain doses with hydrobromic acid three times a day for five days, twice a day afterwards. Small blisters were also applied over the heart-region. There being no improvement, but the reverse, I determined persistently to administer the sulphocarbolate of sodium in thirty-grain doses three times in the day. Carbolized oil, in the proportion of one part of pure carbolic acid in four parts of olive oil, also was rubbed into the chest and the back twice a

day. At the end of a week the general conditions began to improve, and two days after it is noted—that the patient sleeps well and has a good appetite. She still made many complaints of pain, and the mental condition was unstable, but there was a progressive improvement in all the general signs, and after twenty-three days of this treatment appetite was good, bowels regular, temperature normal, and patient asserted that she felt better. She was now in a totally different mental condition; the hebetude seemed quite to have passed away. From this time forward she progressively improved. I omitted the sulphocarbolate and ordered the tincture of perchloride of iron with five-minim doses of tincture of digitalis in infusion of quassia three times a day. The weekly increase of weight was from 8st. 9lb. to 9st. 1lb., 9st. 3lb., 9st. 7lb., 9st. 8lb., 9st. 11lb. successively; and the patient was discharged active, cheerful and bright. The following are the recorded signs shortly before discharge:—Intelligence good; sleeps well; well-nourished and increasing in weight; tongue clean; appetite good; bowels regular; there are no complaints of pain. *Heart:* A systolic murmur is still heard at apex, but is less marked, whilst the diastolic murmur which was heard to the left of the sternum is now scarcely audible. There is no evidence of cardiac hypertrophy nor of dilatation. *Lungs:* No cough nor expectoration; lung-sounds normal. Temperature 98°·5 F.; pulse 76; respirations 22; urine sp. gr. 1020; no notable abnormalities. The urine throughout had been non-albuminous; its specific gravity varied between 1018 and 1030; it offered no points for notice.

I venture to submit two propositions—not by any means that I claim to have proved them—but as worthy of consideration. The first is that severe endocarditis—understanding by this term not the rheumatic form but forms aberrant therefrom and attended with grave symptoms—is due to the influence of septic micro-organisms. The second is that a treatment based upon this view presents probabilities of success. On this second proposition there may be, very legitimately, great differences of opinion. The *primâ facie* case is that a given patient with signs of grave endocarditis shows no signs of amendment until a given drug is administered, and then progressively improves and makes a good recovery. It may be urged that the relation is *post hoc* and not *propter hoc*; that the rest and preliminary treatment, unsuccessful for a long time, may have had some undiscovered influence; that the disease process may have become gradually modified and a restoration to healthy conditions by the simply-aided power of Nature have been brought about. Against this view it may be contended that it is contrary to general experience to find a case manifesting the conditions I have just described recover. Then, as to the agent employed, what is its probable mode of action? So far as I know it is only valuable, directly rather than indirectly, as a poison to micro-organisms. It is an antiseptic readily capable of internal administration. But can an agent capable of killing low organisms be administered in adequate amounts to a higher organism—their host? On this point there seems to be much misconception. It has been stated, and it seems to be accepted by many, that a definite "No" must be given in answer to such a question. I venture to state that such an unsatisfac-

tory dictum is contrary to evidence. Before introducing the sulphocarbolate of sodium as a definite chemical compound and as a therapeutic agent in 1869,* I found that the salt could be administered in large doses without any inconvenience or hurtful results to animals. Two guinea-pigs readily consumed 275 grains of sulphocarbolate of sodium in four days. From the evidence, which I need not further pursue, I concluded that the salt appeared in the tissues as sulphate of sodium, the phenol being liberated. Thus I found that the tissues were rendered antiseptic, the muscular tissue did not undergo ordinary putrefaction, but became desiccated. This observation has been confirmed; but it is not new. Prof. Polli of Milan had found a like result when large doses of the alkaline sulphites had been administered to animals. It must, I urge, be admitted that adequate amounts of an antiseptic agent *can* be administered to a living animal to destroy, or to prevent the development of, micrococci which are the agents disposing to putrefactive change. In regard to the agents which produce the phenomena of septic disease in the living body it must be acknowledged that the conditions are not identical—but they are analogous. Septic micro-organisms differ widely in their behaviour with toxic agents and with conditions of environment, but it is by no means quixotic to attempt to annul their morbific effects by an agent which affects their own vitality. The search for such an agent may be surrounded with difficulties; these may by no means be insurmountable; and one agent may prove the more efficacious in one septic disease and another in another.

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* *Medico-Chirurgical Transactions*, vol. lii. p. 139.

The researches of Dr. Theodore Cash undertaken for the Medical Officer of the Local Government Board,* have a high interest in this relation. Dr. Cash found by experiments on animals that sulphocarbolate of sodium administered to guinea-pigs in no appreciable way controlled the phenomena of tuberculosis as determined by inoculation; but in case of anthrax "the action of large doses of phenol-sulphonate of sodium [identical with the sulphocarbolate] may materially affect the course of the anthrax development." Dr. Cash adds, "the fact of delay in development of the fatal activity of the anthrax virus is of no small interest, and is calculated to raise the hope that further research, which is now being prosecuted, will lead to valuable information on the hitherto much-neglected study of prophylactic medication."

I think I have made out a case for the due trial of the plan of administering the sulphocarbolate of sodium or other suitable antiseptic in sufficient doses in cases of severe endocarditis.

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* Fourteenth Annual Report of the Medical Officer to the Local Government Board, 1884-5, p. 192 *et seq.*

LECTURE II.

MITRAL REGURGITATION.

Morbid Anatomy—Mitral Regurgitation in Anæmia; treatment by Supplementary Alimentation—Mitral Regurgitation in Neuroses of the Sympathetic; treatment by Electricity—Mitral Regurgitation in Acute Fevers; in Rheumatism; in conditions of high Arterial Tension—Treatment of Regurgitation due to valvular imperfection—Digitalis—Venesection—Objections to Digitalis in some cases—Caffeine—Analysis of Cases treated—Convallaria Majalis—Belladonna — Morphia — Urethan and Paraldehyde — Nutrients—General Hygiène and Dietary—Oertel's Rules—Massage—Treatment at Aix-les-Bains—Dr. L. Blanc's Observations.

I HAVE to ask your attention to the subject of the treatment of various conditions of disease associated with a certain imperfection in the mechanism of the heart—an imperfection of closure of the left auriculo-ventricular orifice at the time of systole, occasioning the reflux of a portion of the contents of the left ventricle into the left auricle, the mitral valve being inadequate to close the orifice.

Pathological anatomy teaches that such result may be brought about by several varieties of morbid change:—

1. By dilatation of the left ventricle without structural disease of the valve. So the free borders of the curtains are drawn upon by their circumferential attachments, and prevented from a perfect apposition in systole.

2. By the changes in the valve-curtains, the

tendinous cords and fleshy columns induced by endocarditis, and the processes consecutive thereto. Vegetations about the orifice may prevent its perfect closure. Or the valve being thickened, its segments may be imperfectly coäpted. Or curtains, cords, and columns, any or all, may become shrunken, thickened, fibrous, or cartilaginous from sclerous change. Or from deposit of earthy salts, the valve and orifice may be hard and calcareous.

3. The valve-curtains, cords, or columns may become ruptured, and therefore incompetent. It has been supposed that this may occur from sudden strain in a healthy heart; but Drs. Wilks and Moxon have given strong reasons for the conclusion that there must have been some dilatation, at least, of the left ventricle previously. They consider that this accident is not of infrequent occurrence, and say—"The snapping of an overstrained mitral tendon in a dilated heart we believe to be a relatively very common cause of severe heart-disease, converting the very bearable trouble of a moderate dilatation into a hopeless disablement."*

4. Patches of atheromatous disease may be observed upon the valve, with consecutive degenerative change, rendering it inadequate.

5. Portions of the valve and the surrounding structures may be destroyed by ulceration.

Such are, in brief, the changes which are observed on post-mortem examination to render perfect closure of the left auriculo-ventricular aperture impossible.

Mitral regurgitation is, however, not to be wholly

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* *Cf.* "Pathological Anatomy," by Drs. Wilks and Moxon. Second edition. London: John Churchill & Sons. 1875.

interpreted by pathological anatomy. It is to clinical investigation that we must chiefly look for guidance. We ask ourselves, first, from what sign observed in the living body do we infer that the mitral orifice is incompletely closed in systole? The answer is, from a *consensus* amongst observers, that a murmur heard with the first sound at the apex of the heart, localized at this point, conducted externally towards the left axilla, or to the back in the neighbourhood of the angle of the left scapula, indicates that there is in existence a condition permitting regurgitation into the left auricle. The sign is almost, though not quite, pathognomonic. The only condition with which it is likely to be confounded is, in my opinion, pericardial roughening at or about the apex. I have never known a difficulty about the differential diagnosis in the case of adults, but I have observed such difficulty several times in children. In cases of children I have repeatedly said that the quality, character, and situation of a systolic apical murmur will not declare with precision whether there is exocardial or endocardial disease. My House-Physicians at the North-Eastern Hospital for Children have observed this with me. A murmur which has been ascribed to mitral regurgitation by competent observers has been proved on post-mortem examination to be due to roughening of or fibrinous exudation on the pericardium in the neighbourhood of the heart's apex.

The difficulty of diagnosis is, however, an infrequent one, and we may conclude that in a vast majority of cases the existence of a murmur having the characters which I have mentioned, indicates a condition of mitral regurgitation.

Combined clinical and necroscopic observation, however, soon convinces us that in certain cases, wherein we have determined from such physical sign that mitral regurgitation existed during life, no lesion whatever indicating inadequacy of the mitral valve to close its orifice has been discovered after death. Moreover, in some cases where we have not only observed the sign mentioned, but where the whole category of signs, symptoms, and consecutive changes which experience has taught us to associate with mitral inadequacy has been present, the autopsy has demonstrated no determinate lesion at the orifice.

It will best serve a practical purpose, I think, if we divide the cases in which the signs indicating mitral regurgitation are evident, into clinical groups, discussing the bearing of the collateral phenomena upon treatment in each group. We shall thus consider the cases just as we meet with them in practice.

I. A case presents itself, manifesting signs indicating mitral regurgitation in the subject of marked *anæmia*. We have to inquire whether or no there has been antecedent disease leading up to organic change at the mitral orifice. Supposing such signs are not in evidence, have we a right to assume that actual mitral regurgitation can be induced by the condition of anæmia without concurring causes? The answer is, in my opinion, undoubtedly in the affirmative. In cases of anæmia and chlorosis a murmur is sometimes heard exactly in the site of that indicating mitral regurgitation. I have observed not only this sign, but all the concurring signs of cardiac failure, in a woman who suffered from excessive periodic hæmorrhages per vaginam, associated

with uterine fibroids. I was called to such a case (Mrs. H., aged thirty-nine), manifesting severe dyspnœa such as one meets with in cardiac disease, extensive œdema, and a loud systolic murmur heard at the apex of the heart. The patient was very anæmic from copious hæmorrhage, the cause of such hæmorrhage having been diagnosed by Sir Spencer Wells to be uterine fibrosis. With care, rest, and suitable treatment, she recovered from all the symptoms denoting cardiac disease, and the murmur wholly disappeared. This I consider to have been an instance of what Professor Balfour has termed "curable mitral regurgitation."

In the disease known as *progressive pernicious anæmia* it is common to find an apex-systolic murmur. Such was noticed in four of eight cases recorded by Dr. Byrom Bramwell. In one an observer had diagnosed the case as cardiac dropsy from mitral insufficiency.* In three cases recorded by my colleague, Dr. Stephen Mackenzie, an apex-systolic murmur was noted. Though in many of such cases the murmurs are heard at the base of the heart and over the site of the pulmonary artery, they are, as Dr. Stephen Mackenzie has said, "sometimes loudest at the apex of the heart, conducted into the axilla and heard at the angle of the left scapula. It is remarkable how loud and harsh these bruits sometimes are."†

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* *Edinburgh Medical Journal*; Nov. 1877.

† Clinical Lecture on Idiopathic, Essential, or Pernicious Anæmia: *Lancet*, 1879. *Vide* Gulstonian Lectures on Anæmia, by S. Coupland, M.D., F.R.C.P.: *British Medical Journal*, April 2, 1881, p. 501; and J. H. Musson, M.D., "On Idiopathic Anæmia." Philadelphia. 1885.

A series of phenomena strictly analogous to those just mentioned as occurring in the human subject can be induced in animals by copious bleedings. Dr. Donald MacAlister says: "When an animal is bled till it is feeble, a murmur indicating regurgitation from the ventricle is heard with the heart-sounds. You may inject a proper saline solution to make up the normal quantity of circulating fluid, but still the regurgitation occurs. As the animal makes blood again, so that its muscles are again properly nourished, the murmur disappears."*

And now, assuming that in these cases there is a veritable regurgitation, how is such brought about? The explanation is, I think, given by the careful experiments conducted by Ludwig and Hesse at Leipzig, which have been admirably summarized by Dr. Donald MacAlister.† The mechanism for the closure of the left auriculo-ventricular orifice does not reside in the valve alone; the surrounding muscles of the ventricle have an active share not merely in floating up the valve-curtains, but in reducing the size of the aperture which these valve-curtains have to close. In Dr. MacAlister's words: "As systole begins, the muscles surrounding the ostia contract; and presently, instead of the round gaping orifices of diastole, the valves have to close oval and compressed ones. . . . . The base muscles do their share of the work of closure, the valves promptly complete it." When the muscles of the base are enfeebled, as in the cases which we have been considering, the

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* *British Medical Journal*, Oct. 28, 1882, p. 825.

† "Remarks on the Form and Mechanism of the Heart," *loc. cit.*

valve-curtains are insufficient to close the orifice, because such orifice is wider than usual. It is not that the aperture is dilated, but that it is insufficiently contracted, the aid of the muscles which normally produce such contraction being lost.

Regurgitation may result, therefore, from feebleness of muscle, and restoration to the normal may occur with improved nutrition; but it must be recollected that persistent anæmia or repeated blood-lettings (as shown by experiments on animals) will induce a fatty degeneration of the heart-muscle, a morbid condition which may be irrecoverable.

I think it will be agreed that both for prognosis and treatment it is important that we should be able to make the differential diagnosis between a regurgitation due to feebleness of muscle, the result of anæmia, and organic disease at the mitral orifice. I will suppose that in a case of anæmia presenting a systolic murmur at the apex there is no evidence to lead us to suspect previous valvular disease, and no history of rheumatism. It may be, however, that the regurgitation is not from adynamia of the ventricle, but from an endocarditis of insidious origin, such as I have previously described. Can we rely for guidance on the physical signs? I will mention an illustrative case. I was called a short time ago to a patient at the London Hospital, who was supposed, after the preliminary examination, to be suffering from mitral disease. There was a loud apex-systolic murmur, typical of mitral regurgitation. On delineating the outline of the heart by percussion, however, I noted that there was no notable dilatation such as one would expect to find in organic heart-disease when failure was imminent; for the patient was extremely ill. Noticing the very marked pallor, I suspected

that this might be a case of idiopathic pernicious anæmia, and in confirmation of this view I found the fundus oculi studded with abundant hæmorrhages. I have no doubt, both from these reasons and from the clinical history, that this was a case of mitral regurgitation in association with pernicious anæmia. Unfortunately, the patient being a Hebrew, an autopsy was not performed. I would insist, therefore, on the value of *determining the outline of the heart by percussion* as a means of differential diagnosis in these cases. In anæmia, as I have observed, the heart is not notably dilated.*

In the case I have mentioned as occurring in conjunction with hæmorrhage, I found the *determination of the tension in the arterial pulse* to be a very important means of differential diagnosis. In advanced organic mitral disease—when, for example, dropsy and extreme cardiac dyspnœa have supervened—the arterial tension is usually low (Fig. 11). In the case mentioned I found the opposite indication—the tension, as shown by the sphygmographic tracing, was rather high. It is an unexpected thing, as Dr. Broadbent has pointed out, that "in a disease such as chlorosis, characterized by debility, there should be high arterial tension: but such is the fact."† My experience is in this particular entirely in

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* Dr. Allbutt has found that in progressive pernicious anæmia the heart is not dilated, but simply atrophic. Dr. Theodore Williams has observed that some cardiac hypertrophy often follows anæmia, but dilatation is not evidenced. (*Cf.* Discussion on Professor Balfour's paper, Arguments in Favour of Dilatation of the Heart as the Cause of Cardiac Hæmic Murmurs, &c.: *British Medical Journal*, Aug. 26, 1882, p. 354.)

† *British Medical Journal*, Aug. 26, 1882, p. 355.

accord with Dr. Broadbent's. In progressive pernicious anæmia, however, in its late stages the tension of the pulse is, as Dr. Byrom Bramwell has pointed out, very low.

These two signs, therefore—an area of cardiac dulness not perceptibly greater than the normal, and a heightened tension in the systemic arteries—I consider to be of the greatest importance in differentiating in a very anæmic patient between organic disease at the mitral orifice and incomplete closure from adynamia.

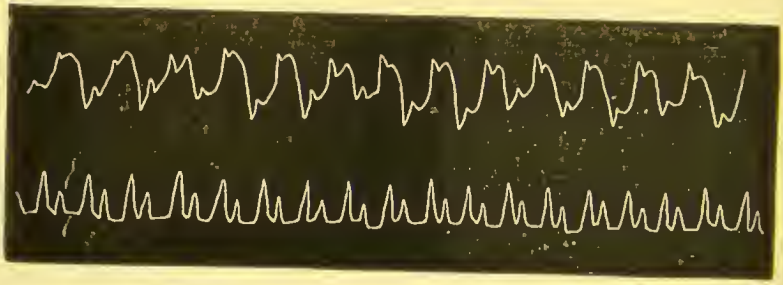

FIG. 11.—Cardiogram and sphygmogram in a case of advanced mitral disease, with free regurgitation.

As regards treatment, such differentiation is important, for I have never known, in the class of cases we are now considering, any marked improvement follow the administration of the usual cardiac tonics, such as digitalis and iron. In the cases attended with hæmorrhage, it is, of course, of the first importance to arrest this at its source. Rest, and the administration of assimilable food, are no less important indications. In this connection I may call attention to the great value I have observed to attach to *supplementary alimentation by the rectum* in such cases. I have long tried the plan of using defibrinated ox-blood for a nutrient enema, as advocated by my friend, Dr. A.

H. Smith, of New York. In comparing results, however, with those in which artificially digested food has been employed, I consider that the balance of evidence is in favour of the latter plan. I have had prepared by Messrs. Savory and Moore mixed peptone enemata—beef, milk, and farinaceous food—which have been proved to preserve in perfectly good condition for long periods. These have the advantage of being available at a moment's notice, it being only needful to render them diffluent with warm water. From two to four ounces are injected slowly into the rectum, and repeated every three or four hours. In many cases I have caused to be added the dried ox-blood (*sanguis bovinus exsiccatus*), in the proportion of a drachm to the ounce. I have lately, however, adopted a simpler plan with good results—using, instead of peptoned food, equal parts of warm milk and cod-liver oil as a nutritive enema.

In the treatment of cases of idiopathic anæmia, I have found no drug-treatment so efficient as the administration of arsenic (Fowler's solution in small doses, gradually increased). I have observed, as has been recorded by others, complete recovery with the disappearance of the cardiac murmur under such treatment combined with rest and careful nutrition.

It has been supposed by Naunyn, Balfour, and others that actual regurgitation through the mitral orifice is in existence in cases where a systolic murmur is observed in the second left interspace near the border of the sternum. I am far from convinced that such view is correct, and prefer to adhere to the opinion that such murmurs are generated usually in the pulmonary artery. A consideration of this debatable question is unnecessary here, as I am dealing

with those conditions in which observers would generally agree that mitral regurgitation was undoubtedly indicated.

II. We will now assume that a systolic apex-murmur is present in a patient showing signs of *a neurosis of the cervical sympathetic*. It has been frequently noted that a murmur at the apex has existed in the subjects of exophthalmic goître (Graves' or Basedow's disease); yet, on post-mortem examination, no disease at the mitral orifice has been discovered. In these cases anæmia may be present, but not of necessity. It is not causally related with the phenomena. Organic heart-disease may coexist, but such coincidence is rare. It is important to recognise—especially with regard to treatment—that in the subjects of Graves' disease mitral regurgitation occurs without valvular lesion. I now wish to draw attention to a point with reference to this curious affection—viz., that, as I have myself observed, the triad of symptoms—the protrusion of eyeballs; the thyroid enlargement; the paroxysmally disturbed, rapid, palpitating heart—can be disunited: and we may observe in a given case a union of two of the groups, or even one group alone. For example: I brought before the Ophthalmological Society a patient manifesting pronounced exophthalmos without thyroid or cardiac symptoms.* I have lately seen in consultation a case manifesting only the cardiac phenomena, the heart's action being very rapid and the paroxysms of palpitation extreme. Again, I have lately observed the case of a lady in whom there is a

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* *Ophthalmological Transactions*, vol. ii. p. 241.

combination of the cardiac and thyroid symptoms without exophthalmos. In each of these cases there was a history of shock, mental anxiety, or nervous exhaustion as a proximate cause. In the last case the cardiac trouble was severe; besides distressing paroxysms of palpitation a loud murmur was manifest at the apex, and extensive œdema supervened. In fact, the case closely resembled one of organic mitral disease. There can be but little doubt, I think, that in these cases there is disorder, if not disease, of the cervical sympathetic, or of certain centres in the encephalon—viz., the centre regulating the cardiac movements, the vaso-motor centres for the head and neck, and the centre for co-ordinating the movements of the globe and the lids. (*See* Note C.) In the cases which I have seen, ordinary tonics and digitalis have been of very little benefit, but great improvement has followed galvanization of the cervical sympathetic. I have employed the continuous current, from twenty to forty elements (Léclanché). One pole may be placed behind the lower jaw in front of the sterno-mastoid, and the other either at a corresponding point of the opposite side, or at the nape of the neck right or left of the vertebra prominens, or above the sternum at the inner edge of the insertion of the sterno-mastoid.

Prof. Charcot has added the weight of his testimony in favour of electricity as a remedial agent in Graves' disease, and has also recognised that in this affection the triad of signs may be disunited, and that there may be one cardinal symptom, such as the cardiac. He recommends that both faradization and galvanism be employed. The faradic current is to

be transmitted through the two carotid regions alternately: the positive electrode is applied to the back of the neck, and the negative strongly pressed over the carotid artery beneath the angle of the lower jaw. Sometimes an immediate change in the colour of the cheek is noticed upon the side through which the current is transmitted, the feeling of orbital tension is lessened, and the temperature reduced. The negative electrode is also passed lightly over the eyelids and over the thyroid and sterno-hyoid muscles, so as to cause some muscular contractions; the thyroid gland is also faradized. Then the continuous galvanic current is applied to the præcordium, the negative rheophore being at the back of the neck and the positive over the inner portion of the third left intercostal space. Under the influence of the current the violence of the heart diminishes. The whole sitting should last for ten or fifteen minutes, and should be repeated every other day. Complete cure requires six months' treatment at least; recovery takes place in a large majority of cases.*

III. I now turn to a third group of cases, and assume that the indications of mitral regurgitation are manifest *during the evolution of certain fevers.* In the course of typhoid fever, for example, a systolic murmur may be discovered at the apex. There is no history of its existence before the attack, but it has

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* *Gazette des Hôpitaux*, 1885, Nos. 13 and 15. Treatment by electricity has been recorded as successful by von Dusch, Chvostek, Moritz Meyer, Eulenburg, Guttmann, Remak, Ancona, and others. *Cf.* Althaus, "Medical Electricity," third edition, pp. 165 *et seq.*, 335, 621; Hayden, "Diseases of Heart and Aorta," pp. 1050 *et seq.*; Ancona, *Giornale Veneto delle Scienze Mediche* (*British Medical Journal*, June 1, 1878, p. 790).

arisen during the course of the disease. M. Hayem has especially studied these phenomena. He says: "In the course, or at the end, of the second week there arises, in a certain number of patients, a bellows murmur with the systole. At the time of its first appearance this murmur may be soft and of little intensity. Its maximum is at the apex in the neighbourhood of the nipple, but it is prolonged towards the base, becoming feebler there. Often this bruit has an intensity and roughness such as may be observed in organic murmurs; or at first of only slight intensity, it may soon become louder, and make one believe in the existence of endocarditis. Moreover, it may vary in intensity from day to day, or may become modified by a change of position of the patient, as one may observe when auscultating in the lying and sitting positions alternately."* In typhoid fever, therefore, it may be an important question as to the nature of such a murmur, and its bearing on treatment. The clinical evidence shows that in the course of the fever the murmur changes its site and fades away, and that it may be accompanied by reduplication of heart-sounds and disturbances of cardiac rhythm. Thus, in the case of a young lady, aged nineteen, observed by myself, there appeared, on the eleventh day of typhoid fever, a soft systolic murmur, left of the sternum, at the third costal cartilage; on the thirteenth day the bruit extended nearly as far as the apex; on the fifteenth it reached the apex; on the seventeenth it was right of the apex, and there was reduplication both of the first and second

* *Cf.* Des Manifestations Cardiaques de la Fièvre Typhoide, par M. G. Hayem: *Le Progrès Médical*, 17 Juillet, 1875, p. 401 *et seq.*

sounds; on the nineteenth, twentieth, and twenty-first days reduplication of the first sound only was heard, the murmur having disappeared.

The murmur, therefore, is an evanescent one. To what is it due? The changes are, according to M. Hayem's observations, not in the endocardium nor pericardium, but in the muscle of the heart. In fatal cases the muscular fibres present a granular and fatty degeneration, or a special form of *vitreous* degeneration; the areas of morbid change are disseminated in an irregular manner here and there throughout the cardiac muscle. There are, besides, a multiplication of the muscular nuclei and an aggregation of cellular elements. In fact, the disease is a form of myocarditis.

It is, I think, sufficiently proven that the murmur occasionally heard at the apex in cases of typhoid fever is due to regurgitation on account of imperfect apposition of the valves of the left or right sides from enfeeblement, by disease, of the muscular fibres in certain areas of the heart-wall. It does not appear that the occurrence of such murmur renders the prognosis more grave; but sudden death, in all probability from myocarditis, may occur in typhoid without any special evidence of direct cardiac impairment previously. Its occurrence, however, should make us watchful, and cases presenting any of the phenomena indicating myocarditis in typhoid should be observed, and treated with a view of preventing subsequent dilatation.

Analogous myocarditis has been described in variola (by MM. Desnos and Huchard),* and in severe forms

* Des Complications Cardiaques dans la Variole, et notamment de la Myocardite Varioleuse: *Union Médicale*, 1870–71.

of intermittent fever as observed in Africa by M. Vallin.*

It is obvious that a recognition of the nature of the alteration which produces a mitral regurgitant murmur in the cases we have been considering must have an important bearing on treatment. We need not fear that endocarditis has arisen as a complication, nor have we to debate as to an anti-rheumatic plan of treatment. The indication is to keep the disturbed muscle of the heart as tranquil as possible, and of course to promote as good a nutrition as the circumstances will permit.

IV. I now come to the fourth group, and assume that a murmur indicating mitral regurgitation is observed in the subjects of *acute or subacute rheumatism*. Attention has been frequently drawn to the fact that murmurs may arise in the course of evolution of the disease, and yet disappear, and patients being free from murmur have been considered to be free from cardiac complication. I have in my former lecture deprecated this as a too hasty conclusion. It may be well to inquire, in the first place, what is the probable nature of these transitory or evanescent murmurs, which are by no means uncommon, for they occur, as the statistics of the London Hospital for 1880 and 1881 show us, in about 10 per cent. of the cases. Rheumatism is a disease notably attended with anæmia. Is it probable that these bruits are of the nature of those which we have considered to be causally related with Anæmia? The evidence collected for me by Dr. Gabbett as to the site of such transient murmurs is, I think, against this view. It is well

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* *Union Médicale*, 1874, pp. 293 and 316.

known that the murmurs heard in connection with anæmia, though sometimes heard at the apex and indicating mitral regurgitation, are far more frequently audible at the base over the site of the pulmonary artery or aorta. Even when heard at the apex they are usually accompanied by other murmurs at the base. In rheumatism, however, the usual site of the evanescent murmur is the apex. The totals for 1881 show as follows:—Transient murmurs in mitral area fifteen, at base and apex seven, in aortic area five, in pulmonic area three. It would appear that a murmur which might suggest an anæmic causation is almost confined to a first attack of rheumatism; after two or more attacks no basic transitory murmurs are recorded. Then as regards the transient systolic murmur in the mitral area, we may ask whether it may be due to myocarditis. If so, it does not resemble in associated phenomena the murmur observed in typhoid, &c. The peculiar perturbations of rhythm are not recorded, and it would appear probable that if there be myocarditis it does not occur in disseminated areas as in typhoid. May it not be that the temporary regurgitation is due to a localized myocarditis, developed in the neighbourhood of the swollen valve or inflamed endocardium? Thus, though the swollen valve might not be in itself incompetent, a temporary incompetence would be produced by the impairment of the force of the muscle. As the myocarditis subsided the valve would become again competent, but probably, in many instances, to present a renewed imperfection when the swelling in the course of time has given rise to fibrous change and consequent retraction. I draw attention to this as a caution as to the expression of my opinion that a valve is sound after a murmur developed

during rheumatism, though the murmur be temporary.

Let us now suppose that owing to rheumatic endocarditis the mitral valve has been rendered incompetent. It is well known that such may be the case, and yet the subject of such incompetence present no sign or symptom of deviation from health. We are familiar with cases manifesting the murmur of mitral regurgitation in childhood, who pass through the period of adult life without suffering from the distresses of cardiac disease, and who, perhaps, ultimately succumb to an affection, the course of which the valvular imperfection has in nowise sensibly modified. In such cases the valvular imperfection has become *compensated*.

Supposing a regurgitation just instituted, the first effect is upon the left auricle, which is now made to contain a quantity of blood greater than normal by so much as gushes into the auricular cavity at each systole. The effect is to distend and to dilate the auricle. The left ventricle, too, is filled more rapidly than under normal conditions, because the blood from the auricle enters it under pressure the moment that diastolic relaxation permits. Such entrance of blood is more free than the normal. Hence dilatation or hypertrophy of the left ventricle, or a *tendency* thereto. The most important of the induced conditions is, however, that of the pulmonic circulation. The reflux current overfills not only the auricle, but the pulmonary veins and the pulmonic capillarics. Against such resistance comes the force of the right ventricle in systole, which, in opposing the resistance, becomes hypertrophied. The hypertrophy of the right ventricle is essentially conservative, and the increased

tension in the pulmonic circulation is an essential condition of compensation. The sign of such heightened tension, and therefore compensation, is, as long ago pointed out by Skoda, accentuation of the pulmonic second sound in the second left interspace.

Observation of the degree of pronunciation of the pulmonary second sound is of the highest importance as regards the treatment of mitral regurgitation. It is in a considerable degree a measure of the amount of such regurgitation. If the aperture caused by incomplete mitral closure in systole be small, the pulmonic tension is only slightly increased, and the pulmonic second sound may not be perceptibly intensified; but if the gap be wide, the tension, supposing the two ventricles to be in an efficient condition of compensatory hypertrophy, is great in the pulmonic circuit, and the second sound in the pulmonary area is very loud. If afterwards the loudness of such second sound is found to diminish, such sign is of very high importance. It suggests that the compensatory hypertrophy of the right ventricle is beginning to fail, that dilatation is in excess, and that the tension of the blood in the pulmonary artery is reduced by so much as regurgitates through the tricuspid orifice. Of course, the other signs of tricuspid regurgitation should be taken in conjunction with this, but I know no sign which is so valuable a guide for treatment.

As the left auricle is overfilled in proportion to the amount of blood regurgitating, so is the aorta, and from it the systemic arteries, ill supplied. A diminution occurs in the normal quantity of blood propelled to the tissues, while in the veins circulation is retarded and the normal content is augmented. There are arterial anæmia and venous plethora. The institution,

however, of compensatory hypertrophy of the right ventricle rectifies the ill supply to the aorta. The increased pressure in the pulmonic circuit at the time of systole opposes the reflux into the auricle, and the current thus opposed is urged in normal amount into the aorta. So, even supposing that the force of the left ventricle be not augmented, increased force of the right may restore the equilibrium by inducing a pressure in the auricle equivalent to that afforded by a competent valve.

As regards the mode of production of compensatory hypertrophy, I would draw attention to an excellent chapter in Dr. Milner Fothergill's work.*

The practical question which it becomes us to answer, when a patient comes before us who presents signs of mitral regurgitation the legacy of rheumatic endocarditis, is—Is this valvular imperfection duly compensated or not? Subjective symptoms may tell us of such want of compensation, but they are often deceptive. In addition to the auscultatory sign I have mentioned, we may get valuable evidence from the use of the sphygmograph and cardiograph. The former may tell us of a fairly normal tension in the systemic arteries or otherwise; the latter, by recording the duration of systole and diastole, may inform us how far the normal rapidity of filling of the ventricle is exceeded, and thus may give evidence of the amount of regurgitation.

Supposing that we are satisfied that there is due compensation, medicinal treatment may be entirely unnecessary. I have no doubt that a vast amount of

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* "The Heart and its Diseases, with their Treatment, second edition, chap. v. p. 96. London: H. K. Lewis. 1879.

injury has been done to patients by a shaking of the head of the auscultator over the subject of a mitral murmur, who, perhaps, was no worse at the time of examination than he was ten, twenty, or thirty years before, and who might continue uninfluenced for harm by his cardiac complications all his days. He should be cautioned against over-strain, against exposure, and against irregularities of diet, &c.; he may be better occasionally for treatment by iron tonics, cod-liver oil, or strychnine, but any special *cardiac* treatment is out of place.

Not so, however, if there is evidence that compensation is beginning to fail. Such evidence is afforded by a disturbance manifested in different modes in different patients. In one there will be palpitation, irregularities of heart's action, oppression at præcordium, heaving impulse or troubles directly referred to the heart itself; in another difficulties of breathing, variable, but increased by exertion; in another dyspeptic ailments and the results of venous congestion of viscera; in a third the gradual oncome of dropsy. Or the failure of compensation may be first evidenced by an acute attack of inflammation of the lung. We find in such a patient pyrexia, dyspnœa, and the physical signs of a limited pneumonia. On examining the heart we obtain evidence of mitral regurgitation. Then the clinical history teaches us that the pneumonia presents characters which differentiate it from the forms which we observe in those who are not the subjects of cardiac disease. The outline of percussion dulness is clearly defined, often wedge-shaped; the signs indicate the density of a lung affected with croupous pneumonia, but not the extent of area involved in such a case. The sputum

differs from the rusty viscid material of ordinary pneumonia; it is frothy, and in many cases, having continued thus for a day or two, is suddenly found to be bright with florid blood. These signs indicate infarction of a branch of the pulmonary artery, and they may be the first sign which demonstrates to us the failure of compensation in cases of mitral regurgitation. In the enfeebled right heart coagula have formed, which, projected into the pulmonic arterioles, have given rise to the symptoms I have mentioned and to the appearances which, when discovered at the necropsy, have been in some cases designated pulmonary apoplexy. These, then, are among the signs which, when met with in a given case, announce to us that compensation is disturbed. We may have opportunities of watching the downward course: how the left ventricle becomes more and more dilated, how the right chambers yield also, and the venous system becomes engorged—a lesson, perhaps, pointed by the increasing size of the liver, as well as by distressing signs of dyspepsia; and then, how the over-dilated right ventricle permits regurgitation through the tricuspid orifice. This is a slight sketch of the occurrences when a heart affected with an imperfect mitral valve, permitting regurgitation through the mitral orifice, begins and continues to fail on account of the inadequacy of its muscle to overcome the difficulties. But these are by no means all the circumstances with which we may have to deal in any given case. There may be engrafted difficulties: the fires of the old endocarditis may be relighted, pericarditis may be manifested, and in both these conditions, I consider, myocarditis, which of course tends extremely to enfeeble the muscle, is in some degree an

almost constant concomitant; or pleurisy, a frequent association with cardiac cases, may occur; or affections of other organs, especially the kidneys, may increase the dangers. Such are the difficulties which we are called upon to endeavour to overcome by treatment. Now, leaving all questions of general management, what are the special drugs on which we can rely?

1. *Digitalis.*—This is our first resource, and nearly all our patients are treated by it when faults of compensation are announced to us. There is yet some lingering of the old timidity which, regarding digitalis as a sedative and depressant of the heart, would withhold it when the heart is weak. Accurate investigation has shown that digitalis increases the force of the cardiac muscle and tends to cause the arterioles to contract, by a combination of these actions raising the blood-pressure within the arteries.* In a large majority of cases the careful administration of digitalis, combined with measures to promote a good general nutrition, when the early signs of imperfect compensation present themselves in cases of mitral regurgitation, is followed by such good results that it is unnecessary to seek for another agent. After a short period compensation may be restored, and then only general tonics and good dietary and management may suffice to maintain it. In a very considerable number of cases of mitral regurgitation, however, small doses of digitalis may be continued for long periods. My experience quite agrees with that of Dr. Broadbent, who says: "In mitral incompetence digitalis may be given almost indefinitely, and patients

* Brunton: "Textbook of Pharmacology, Therapeutics," &c., pp. 225, 235, and 913. London: Macmillan & Co. 1885.

often take it for years with obvious advantage."* It is quite otherwise in mitral stenosis, as we shall see hereafter.

Digitalis slows the heart by lengthening the diastolic pause; so not only does it give rest to the wearied cardiac muscle, but—as this muscle is nourished only during such diastolic pause by the blood which then enters through the coronary arteries—it directly ministers to its nutrition. It is a matter of common experience that digitalis, especially when combined with iron, strychnine, cod-liver oil, and other tonics, restores the *status quo ut ante* when, in a patient manifesting a mitral systolic murmur, the evidence shows that compensation is beginning to fail. As, however, with every other medicinal agent, caution must be used in the administration. As regards *dosage*, a certain golden mean has to be observed. The often repeated maxim concerning the middle way points its lesson again :

"Levis alit flammas : grandior aura nocet."

A little over a suitable dose may induce nausea, vomiting, anuria, irregularity of pulse, and, instead of slowing, an enhanced rapidity of heart's action. Whilst a dose which produces a favourable result is constant and discoverable in regard to a large majority of patients, in a minority such dose is inconstant and even unattainable.

As regards the preparation used, we may have differences of result; and we know that, as in the caso of so many vegetable products, the energy of different

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* *International Journal of the Medical Sciences*, Jan. 188 p. 85.

samples may vary. The pharmacopœial equivalents of the officinal drugs P.B. are as follows:—

One grain of the dried and powdered leaves = one-third of an ounce of the infusion = eight minims of the tincture.

Practically, I consider the tincture most reliable, and that usually in small doses (ℳv. to ℳx., increased only in exceptional cases, and then occasionally reduced). Next in value I esteem the powdered leaves (gr. ss. ad gr. ij.), the combination of which with alkalies is very useful.

In some cases, even by increasing the dose no apparent influence appears to be exerted by the drug: then digitaline, especially when hypodermically injected, I have observed to give in many cases good results. I usually employ the hypodermic discs, made by Savory and Moore, which contain $\frac{1}{100}$ gr. of pure soluble digitaline in each, the dose for an adult being usually two discs—*i.e.*, $\frac{1}{50}$ grain. The granules of digitaline (Homolle), containing each $\frac{1}{65}$ grain of the active principle, are much used in France for internal administration.

In a child of ten years of age, with dropsy and great distress from mitral regurgitation, I found, after each injection of one-hundredth of a grain of digitaline, hypodermically, at intervals of four hours, the pulse-rate reduced by eight per minute almost immediately. In this case recovery took place from the urgent symptoms, and the child was sent to a convalescent home. She relapsed, however, and died three months afterwards when away from our observation.

When the right ventricle has become dilated so far that there is marked tricuspid regurgitation, the beneficial action of digitalis is by no means so decided.

Nevertheless, in some cases, especially when occasional purgation is a part of the plan of treatment, the signs of tricuspid regurgitation may pass away, as shown by the following case :—

Case I.—Alice B., aged eleven, under my care at the North-Eastern Hospital for children, manifested mitral regurgitation with dropsy, and marked venous pulse was seen in the left external jugular. Treatment consisted of six-minim doses of tincture of digitalis three times a day. The child had taken previously, as an out-patient, four-minim doses with four grains of ammonio-citrate of iron three times a day. After twenty-one days all severe symptoms had passed away; there was no venous pulse, and the case was discharged as convalescent two days afterwards.

In other cases no such favourable result attends. In fact, as *à priori* consideration might suggest, any increased power of systole which the digitalis may bring about serves the more to force back the blood through the imperfect tricuspid orifice into the venous channels. But yet I have seen good results when the administration of digitalis has been combined with abstraction of blood by leeches or cupping.

Case II.—Maria W., a child of ten, manifesting mitral and tricuspid murmurs with percussion-evidence of greatly dilated right ventricle; after rest in hospital for a fortnight and administration of tincture of digitalis in four-minim doses with tincture of the perchloride of iron (♏x.), and a single leech applied to the epigastrium every other day for fourteen days, it was noted that the dulness over the right cavities receded to the mid-sternal line coincidently with general signs of amendment.

I prefer very small abstractions of blood, repeated

every two or three days, to larger bleedings at longer intervals. In a case under my care at the London Hospital this lesson seemed to be pointed, though the recovery was very satisfactory.

Case III.—*Mitral and tricuspid regurgitation—Treatment by perchloride of iron and digitalis, and by casca, without benefit—Treatment by digitalis and abstraction of blood by leeching followed by great improvement—Thrombosis of subclavian vein possibly superinduced by the bleeding.*—Alice F., aged eleven, was under my care for mitral and tricuspid regurgitation, with great and advancing œdema, orthopnœa, and cardiac distress. She was treated by twenty-minim doses of tincture of perchloride of iron, with five minims of tincture of digitalis. After twenty days, tincture of casca was substituted for digitalis, with no apparent benefit. Digitalis was then resumed as before, and, considering the great distension of the right chambers, six leeches were applied to the chest. Great relief of dyspnœa followed, and œdema became less. Improvement was maintained for ten days, and then urgent dyspnœa and signs of greater dilatation of right chambers occurred. Casca was again tried, and this time with some apparent benefit. Purgatives (pulv. jalapæ co. ʒss.) were also administered, but still the grave signs of right-ventricle engorgement continued. Again six leeches were applied to præcordium. A few days afterwards the right subclavian vein was found to be plugged, and the whole arm and forearm became enormously swollen. It seemed to me possible that the abstraction of blood, by rendering coagulation more easy, had perhaps disposed to the thrombosis. Nevertheless, I was convinced that the cardiac trouble was

sensibly relieved by the leeching, and this was repeated, and saline diuretics and digitalis again administered, in doses increasing from ℥v. (℥vij., ℥ix., ℥x., to ℥xx.). Under this treatment there was gradual but very marked improvement. After five days of the full dose of digitalis it was altogether omitted for ten days, and then resumed in ten-minim doses. All the urgent symptoms passed away, the enormous swelling of the arm due to the venous thrombosis entirely subsided, and the patient was discharged convalescent and able to walk with comfort after having been in hospital for six months.

As I have before said, however, the action of digitalis in cases of mitral regurgitation is not always favourable, and it becomes us to inquire what are the drawbacks to the drug. These are manifest even in the early stages of failure of compensation in a minority of the cases. With some patients it does not agree, and cannot be made to agree. It may induce faintness and sickness. In children sometimes vomiting is induced, and it cannot be persevered with. In other cases, though this symptom be not manifested, the drug, instead of increasing the force and decreasing the rate of the pulse, actually increases the feebleness and the rapidity. In some, instead of acting as a diuretic, it diminishes the quantity of urine excreted, and in a few instances there may be insomnia, restlessness, and nervous disturbance. These signs of intolerance of digitalis in cases of mitral regurgitation are rare, but they are sufficient to make us cautious. It is, I think, a good rule, and one that I always adopt, never to give an adult a larger dose than five minims of the tincture (or its equivalent in infusion or the powdered leaves) three times in the

day for a longer period than a week without any observation. Then if tolerance is assured the patient may continue the treatment, or the dose may be cautiously increased.

It is to be remembered that the effects of digitalis may last longer than the period of its administration. Mr. Raven, of Broadstairs, has recorded the case of a woman, aged sixty-seven, with dilatation of the left ventricle and anasarca, in whom fifteen minims of tincture of digitalis administered every four hours for five days induced diuresis and the relief of the anasarca, but symptoms of intolerance (nausea and vomiting) showing themselves, it was omitted, effervescing salines being substituted. The pulse, which had been quick, weak, and irregular, became slower, and ten days after the suspension of the digitalis it had fallen to 40 per minute.* It is in the later stages, however, that the failure of digitalis is most marked. Its power of increasing the force of the left ventricle seems to be gone; the right cavities continue to dilate, dropsy may be manifestly increasing, and yet the agent in all combinations with ordinary diuretics fails to increase the outflow of urine. Then we turn perforce to other agents, such as

2. *Caffeine.*—This is the highly nitrogenized crystalline principle, occurring in colourless silky needles, obtained from coffee, tea, or guarana, and existing in other vegetable products—*e.g.*, the kola-nut. Caffeine is said to be a stimulant of the medulla and cardiac centres, to quicken the pulse and respiration, and to raise the blood-pressure when given in moderate doses. It may induce irregularity and intermittency of pulse; it is classed as a stimulant of the cardiac muscle. It

* *British Medical Journal*, Nov. 24, 1883, p. 1015.

acts as a diuretic, though not invariably so.* Many observers have testified to the beneficial effects of caffeine in various forms of cardiac disease, but there has been by no means a consensus as to its value and as to its mode of action. Francotte found that whilst caffeine increased neither the water nor the urea excreted in the urine in health, it had a pronounced diuretic action in cases of cardiac disease. Riegel of Giessen concluded that it produces the best effects of digitalis upon the circulation, that it is more rapid than digitalis in its action, is not cumulative, and may be administered to the feeblest person.† The following is the recent utterance of Professor Jaccoud. The effects of caffeine "are identical with those of digitalis; slowing of the heart pulsations; augmentation of its force of contraction; diuresis; no nauseous effects; no cumulative action. This drug, therefore, does not necessitate an incessant watchfulness. You can employ it in cardiac cases where the kidneys are affected."‡

As to mode of administration. Pure caffeine is soluble in from 80 to 100 parts of water; its solubility is increased by acids. I have generally employed the citrate, which is freely soluble. It has been objected that this is a doubtful salt, but this objection is of small importance if the proportions of caffeine and citric acid used in its manufacture are definite, the only important function of the acid being to render the salt easy of solution. I employ it in from three-grain to five-grain doses, dissolved in the ordinary

* Brunton, *loc. cit.*, p. 800.

† *Vide* "Cassell's Year-book of Treatment for 1884," Dr. Mitchell Bruce's summary, p. 3.

‡ Cardiopathies: *Semaine Médicale*, Jan. 13, 1886, p. 10.

saline mixture—diluted liq. ammoniæ acetatis. The dose is generally administered three times in the day, but in some cases once only. Instead of the citrate, the pure caffeine may be employed, dissolved in solutions of benzoate or salicylate of sodium; in these it dissolves freely, and thus a concentrated solution may be made for hypodermic injection. The following is a good formula for internal administration: Pure caffeine and benzoate of sodium, of each one drachm; distilled water, six fluid ounces. Half an ounce contains five grains of pure caffeine.

I now turn to the evidence, in cases under my own care, of mitral regurgitation in which caffeine citrate was administered. It is to be borne in mind that all these were cases of great gravity, in which the resources of ordinary treatment had been for the most part exhausted.

1. *Effects on the Excretion of Urine.*—In the following table insignificant variations have not been recorded. The signs < and > indicate a gradual daily increase to, or a gradual daily decrease from, the amounts stated.

TABLE I.—*Showing the daily amounts of Urine, in ounces, in cases of Mitral Regurgitation, treated by Caffeine Citrate.*

Case.	Before caffeine.	During administration of caffeine.	After caffeine.
1	12	36, 40, 114	180, 172, 114, 68, 57
2	—	24, 42, 47, 52	40, 32, 28
3	—	32, 64, 112, 117	—
4	10, varying to 20	20, 30, 36	48, 20, 32 > 15
4*a**	—	16 < 27, 65 > 36, 10	—
5	15, 20, 17	25, 20, 10, 25	—
6	50, 18, 15	30, 34, 20, 25 > 15 < 26	18, 14, 20 > 10 < 15, 20
6*a**	—	20, 18, 15	—
7	17	35 > 12 < 30, 25	10
8	25, varying to 36 > 24	30, 29 > 11 > 6	—

* Readministration.

The evidence of these cases proves the citrate of caffeine to be, in cases of mitral regurgitation, a powerful diuretic. It is shown that the amount of urine passed during a considerable portion of the period when the drug was administered was generally in excess of the diurnal amount passed previously. In some cases the effect is very striking; for instance, in Cases 1 and 3, in which the daily amount ran up in the one case from 12 oz. to 114 oz., and in the other from 32 oz. to 117 oz. In both these cases ten-minim doses of tincture of digitalis were administered with the caffeine citrate, in the first case in three-grain, in the second in five-grain, doses three times a day. It is also, in my opinion, indicated that the influence of the drug as a diuretic may be prolonged beyond the time of its actual administration. Cases 1 and 4 tend to show this, and to indicate that the dictum that caffeine is not cumulative in action must be reconsidered. The cases, however, abundantly prove another proposition—that the diuresis produced by the drug is not invariably salutary, and that the free outflow of urine is not an index of rehabilitation of the general vital powers. In Case 1 the effects were remarkably favourable; there existed extreme ascites and œdema in a woman of fifty-three, the left ventricle being much dilated and hypertrophied; then occurred amelioration and disappearance of all the symptoms, and the patient left the hospital feeling well. There can be no doubt that here the effects were rapidly beneficial. A like result was manifested in Case 2, in which there was evidence of aortic obstruction as well as mitral regurgitation. This case was subsequently treated by convallaria, but the maximum of diuresis was markedly during the *caffeine* period. This patient recovered from all her

very distressing symptoms, and went out feeling well. In Case 3, however, one of extreme severity, in which pericarditis, signs of embolism, and renal complication occurred, the patient died at the very time that the amount of urine passed in the day had reached the high figure of 117 oz. May prolonged administration tend to diminish or exhaust the diuretic effect? In Case 4 the second administration was followed by a steady and gradual increase to a maximum daily excretion of 65 oz., but the administration being continued the outflow fell to 36 oz., and then to 10 oz. In this case aortic disease coexisted; the patient died. In Case 6 there was a slight diminution under the protracted influence, but here there were very severe complications—viz., empyema and renal disease; this patient died, death being, one might say, inevitable. In Case 8, in which death occurred, there was a steady diminution of the urinary outflow during the administration; but here, in a woman of sixty-four, great ascites and œdema existed, with advanced granular disease of the kidneys. Considering that in all these cases the severity of the complications might in themselves constitute a constant and progressive cause of enfeeblement of cardiac muscle, we should not conclude that the urinary inadequacy was due to any action of the drug itself; it might with so much probability be due to a gradual extinction of the powers.

2. *Effects on Pulse and Respiration.*—The following table indicates the results :—

TABLE II.—*Showing rates of Pulse and Respiration in cases of Mitral Regurgitation treated by Caffeine Citrate.*

Case	Before caffeine.	During administration of caffeine.	After caffeine.
1	Pulse 117	100, 94, 96	95
	Respiration	30 > 20	—
2	Pulse	92 > 56	74 > 57, 70, 72
	Respiration	30 > 23	21
3	Pulse	120, 144, 132	—
	Respiration	32, 36, 30, 28	—
4	Pulse 72, var. to 84	96, 112	—
7	Pulse 78 ,, 90	96	120
	Resp. 48 ,, 36	36	54
8	Pulse 100 ,, 114	*	—

* Became quick, small, and weak. Insomnia. Became worse, and died.

It will be noted that the data in two of the cases have been omitted; this has been because they were variable or doubtful. There is evidence, however, as regards some of the cases, that the rates both of pulse

FIG. 12.—Sphygmogram in a case of mitral regurgitation, with œdema and ascites.

FIG. 13.—Sphygmogram in the same case after five days' treatment with caffeine citrate.

and respiration were reduced under treatment by caffeine. In Cases 1 and 2 the influence was very decided. The sphygmogram taken shortly after admission (Fig. 12) shows with insufficient volume a

great irregularity with interpolated systoles. After five days of treatment the second sphygmogram was taken, and it is seen that the pulse has become nearly regular (Fig. 13). In Case 2 the combined effect of convallaria and caffeine is well shown. The pulse, which at commencement of treatment was 92, had now, after six days of treatment, not only become reduced in frequency to 52, but had acquired marked evidence of tension, as shown by the sphygmogram (Fig. 14). In the other cases, complicated as I have stated them to be, there was no such favourable reaction, though in Case 7 it is shown that on the omission of the caffeine the rate of pulse and respiration rose in very considerable degree.

FIG. 14.—Sphygmogram in a case of mitral regurgitation treated by caffeine and convallaria in combination.

3. *Effects on the Temperature of the Body.*—In Case 1 the temperature was nearly normal throughout. In only one case (3) was there a rise of temperature under caffeine; then it was from subnormal to 100° F. In the other cases the reduction was from a subfebrile temperature to normal or subnormal. In Case 7 the temperature previously to the administration varied between 99° and 102°, and during the administration between 98° and 100°. It may therefore be concluded that in such cases as we have been considering, caffeine tends to depress the temperature.

I think we are justified in concluding that caffeine, in the treatment of cases of mitral regurgitation in which failure of compensation has occurred, is a valuable agent; that it is a powerful diuretic, and is therefore very valuable in cases manifesting dropsy; that it tends to increase the force of the heart, to calm the respiration, and reduce the temperature; but that it fails in some cases to be of benefit, even though it may manifest its diuretic effect. Like other heart-tonics, it fails especially in pericarditis, where probably the direct enfeebling agency of the disease upon the myocardium is a cause which operates against it.

I now turn to another remedy of comparatively modern introduction—

3. *Convallaria Majalis.*—This plant, the well-known lily of the valley, has long been used for the treatment of dropsy in Russia, in the form of an infusion of the flowers and leaves. M. Germain Sée, of Paris, made a careful study of it as a therapeutic agent. Its therapeutic efficiency resides in the principle convallamarin, a glucoside, which may be administered in doses of from half a grain to two grains daily; on account of its cumulative tendency only one dose of convallamarin should be administered each four hours. The following are its preparations and administrations:—1. Extractum convallariæ, an aqueous extract of the flowers and stems (two parts) and roots and leaves (one part), the dose being from two to eight grains. 2. Extractum convallariæ fluidum, dose from two to ten minims. 3. Tinctura convallariæ, dose five to thirty minims. Convallaria is classed with digitalis as a stimulant of the muscular fibre of the heart, and is said to act more slowly and more

persistently than the latter. Within the last two years convallaria has been extensively used in the treatment of various forms of cardiac disease. The experience of various observers in regard to it is very contradictory; so great is the discrepancy that it has been suggested that the activity of the plant varies with the locality in which it is grown. If this be a difficulty, of course it can be obviated by the employment of the active principle—convallamarin. According to many observers—*e.g.*, Germain Sée, Rochefontaine, A. H. Smith, Labbée, Frederick Roberts, Ott, and others—very valuable results are produced by the drug in cardiac diseases. On the other hand, Leubuscher has declared that it has proved in his hands worse than useless as a remedy. Heller has also given an unfavourable report.* Professor Jaccoud says concerning it:—"It is a very untrustworthy medicament, and many cases are quite refractory in regard to it. You must not count upon it, and in cases of urgency you would be wrong to fill up by its administration the intervals of a digitalis course; these you should rather confide to caffeine. If this latter is not well borne, we have no other resource than convallaria; but, I repeat, do not count too much upon it."† In estimating the value of such a drug, it is most important, in my opinion, to group the cases. Those on which the conclusions of the various observers have been based were very different forms of heart disease and heart disturbance.

I now proceed in the same manner, as in the case

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* See Dr. Mitchell Bruce's Summary in "Cassell's Year-book of Treatment for 1884," p 5 *et seq.*

† *Semaine Médicale*, Jan. 13, 1886, p. 10.

of caffeine, to inquire concerning the influence of convallaria in mitral regurgitation. In the cases comprised in the following table convallaria was administered in doses of five grains of the extract or twenty minims of the tincture three times in the day.

TABLE III.—*Showing the daily amounts of Urine, in ounces, in cases of Mitral Regurgitation, treated by Convallaria.*

Case.	Before convallaria.	During administration of convallaria.	After convallaria.
1	20	21, 25, 30 > 16 < 30 > 20	30 > 20 < 30, 26
2	20, 30	35, 17, 22, 20, 27, 22	35, 22, 27, 30, 25
3	—	45, 48, 40 < 60, 69, 60 > 52 < 60	—
4	20, 40	45, 64 > 10	—
5	13 < 35 > 10 < 80 > 35	20, 28 > 15	—
6	—	17	35, 30 > 10

If we took the evidence of these cases as indicating the action of convallaria in cardiac disease generally, we should conclude that it is a feeble diuretic. I must ask that judgment be withheld until after consideration of its action in mitral stenosis. It is seen that in four of the cases a slight diuretic action was soon manifest; the maximum diuresis was attained in one, two, four, and eight days; except in Case 3, there was on continuation of administration a tendency to a diminished excretion. In Case 6 the drug was only given for two days; and then, as urine was very scanty, digitalis and caffeine were substituted, with the result of a very decided, but temporary increase. So far as these cases show, the influence of convallaria as a diuretic in cases of mitral regurgitation is far inferior to that of caffeine.

The effects of convallaria on pulse and respiration in cases of mitral regurgitation are indicated in the following table:—

TABLE IV.—*Showing rates of Pulse and Respiration in cases of Mitral Regurgitation treated by Convallaria Majalis.*

Case.	Before convallaria.	During convallaria.	After convallaria.
1	Pulse	120 > 104 < 120	120 > 108
2	Pulse 114	112 > 108	104 < 124
	Respiration 36	34 > 24	34 > 20
3	Pulse	72	—
	Respiration	20	—
5	Pulse 134, 140 > 104 > 76	70	—
	Respiration 28 < 36 > 24	No imprt. of dyspnœa	—
6	Pulse	Varying betw. 78 & 90	Var. betw. 96 & 120
	Respiration	„ „ 36 & 48	Increased to 54
7	Pulse	96, 120 > 108	—
	Respiration	22 < 40 > 20	Much imprvt. foll.
8	Pulse 120, 98, 88	108 > 84, 90	84 < 108 > 72
	Respiration 27	36 > 30	28, 24, 20

It is seen that, as a general rule, the rates of pulse and breathing are reduced under the influence of convallaria. That the force of the heart and tension of the pulse coincidently with a good regularity of rhythm *may* be brought about I have graphic evidence to prove. Case 5, however, shows that, even though the pulse-rate be very greatly reduced, there may be no relief from the embarrassment of respiration. This case was one in which there was much cardiac dilatation, and it was complicated by embolism of the right axillary artery. The pulse-trace manifested much irregularity and pronounced dicrotism. Case 7 was complicated with aortic obstruction and regurgitation. Three grains (a smaller dose than that administered in all the other cases) of the extract of convallaria

were given three times a day; here, though there was during treatment a temporary increase of the rates of both pulse and respiration, the rate of the latter became notably reduced. This patient was discharged after having manifested much improvement.

Effects on Temperature.—In only two cases was there a rise of temperature under the treatment by convallaria; in neither did it rise above 102°, and in one it fell to 99° at the end of the period of treatment. Generally there was after commencement of treatment a slight fall, and this sometimes occurred suddenly. The lower readings persisted for some days after the cessation of convallaria, and then as a rule the temperature rose again or became irregular.

General Effects.—Cases 1, 4, 5 and 6 manifested no signs which seemed to me to indicate that the drug exerted any marked influence for good, or that it was in any way superior to digitalis. Two of these cases died, one of them being complicated with pericarditis, pleuritis, and pulmonary infarction; the others tided over their difficulties, and were ultimately discharged from hospital. In Case 2, where aortic disease was combined with mitral, much general improvement was manifested two days after the termination of the treatment by convallaria; one week afterwards there was relapse with extreme dyspnœa and death. Case 3, which was also complicated with aortic disease, manifested great improvement; Case 7, with a like complication, also; and in Case 8, which was of the hopeless form of post-partum endocarditis, manifested improvement during the period of convallaria treatment, the temperature then being notably

subdued, to manifest irregular rise and fall subsequently.

My general conclusion is that in convallaria we have a drug which may be occasionally used with advantage in cases of mitral regurgitation; that it should be continued for no longer than weekly periods without interruption; that in cases manifesting dropsy it should be accompanied with caffeine; but that for general and systematic administration in mitral regurgitation it will not (except at intervals) usefully supplant digitalis.

4. *Belladonna* is, I think, only useful in the treatment of failure of compensation in cases of mitral regurgitation when combined with, or *occasionally* substituted for, digitalis. The hypodermic injection of one-fiftieth of a grain of digitaline, with one-sixtieth of a grain of atropine, I have found very satisfactory.

Small doses of belladonna raise the blood-pressure by stimulating the vaso-motor centre in the medulla, and possibly also by increasing the force of the cardiac contractions, but on this latter point the evidence is doubtful. Belladonna cannot be regarded like digitalis as a cardiac tonic, suitable for frequent or prolonged administration. It is rather a cardiac stimulant.

A very long experience testifies, however, to the value of the belladonna plaster placed over the heart-region. It is seldom that a patient who has suffered from palpitation or from pain referred to the heart-region, or who has begun to manifest the distress arising from a failure of the power of the ventricles, has not been advised to resort to the time-honoured plan of applying a belladonna plaster over the præcordium. It is impossible to resist the evidence

that this has contributed to improve the conditions—and we may ask, how? Probably, in the first place, by the mere effect of local warmth and pressure. In palpitation and heart-pain, relief may be afforded by an ordinary adhesive plaster over the præcordium, or by the application of a flannel bandage to the chest. No doubt, however, the belladonna plaster is *more* efficacious, and patients who have worn one for a considerable time find a marked benefit after the old one has been removed and a new one applied. There can be no doubt of the absorption of the belladonna, not only with the result of producing an analgesic effect locally upon the cutaneous nerves, but an anæsthetic influence upon the heart itself. Schiff found that a dose of atropine, slightly more than that sufficient to cause dilatation of the pupil, so reduced the sensibility of the heart to changes of blood-pressure, that such pressure might be artificially increased to three times the normal, and often reduced to one-half or even one-third, without disturbance of the rate of the pulse.* One may readily understand how that belladonna taken internally in small doses may act indirectly as a cardiac tonic by subduing tumultuous action, and how it may be beneficial in some cases, as practical experience proves it is, when combined with digitalis. It is not advisable, however, to continue its administration for protracted periods.

5. *Morphia.*—Judiciously employed, I consider that this is one of the most valuable of agents, or rather adjuncts, in the treatment of the distress, especially

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* *Cf.* Brunton's "Pharmacology, Therapeutics, and Materia Medica," second edition. London: Macmillan, 1885, p. 257.

the dyspnœa and insomnia, attendant upon failure of compensation in cases of mitral regurgitation. I am strongly of opinion that it should not be administered by the mouth, but by hypodermic injection. When given by the mouth it disagrees, just as opium frequently does; whereas, administered hypodermically, it calms the most distressing dyspnœa, without inducing, so far as my experience goes, any ill effect. The value of the hypodermic use of morphia in the distress of heart disease was brought before the profession, in his usual forcible and able way, by Dr. Clifford Allbutt in 1869.* I entirely endorse his view of the value of the remedy and its innocuousness usually in cardiac failure. I have found it valuable to combine the morphia (usually a hypodermic dose of one-third of a grain) with atropine (one-sixtieth of a grain), or digitaline (one-fiftieth of a grain).

6. *Urethan.*—A medicine which should act in cases of cardial disease simply as a hypnotic has long been a desideratum. In very severe distress, morphia employed hypodermically is the only agent which has seemed to me adequate. In many cases, however, insomnia uncomplicated is a marked symptom, and one that impedes the good progress of the case. The bromides are generally quite inefficient, and chloral tends to induce some mental instability, if not sub-delirium. In such conditions *paraldehyde* has been employed. It may be administered in doses of from 30 to 60 minims in diluted syrup, or in almond mixture, or it may be given in capsules, for it has an unpleasant taste. In physiological action it resembles

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* *Practitioner*, 1869, p. 342.

chloral, but it slows the heart and is said to increase its energy of action. The most satisfactory agent which I have hitherto employed is *Urethan.* This substance, ethyl carbamate, is in clear crystals, freely soluble in water, the solution having a slightly saline but by no means unpleasant taste. In doses of 15 or 20 grains at bedtime, I have found it induce a calm natural sleep, lasting in a case of severe cardiac failure for at least five hours, the patient being manifestly refreshed on waking. It has produced no adverse symptoms whatever. It is, I consider, a distinct gain to cardiac therapeutics.

7. *Means for Promoting Nutrition.*—In addition to such special cardiac treatment, general measures should be adopted for securing improved nutrition. The heart-muscle must not only be preserved from wasting, but it must also be fed. The problem of administering a due amount of nourishment is often a difficult one. Sir William Roberts has recommended in the gastric crises of cardiac disease, when there is an almost complete inability to take food, the use of peptonized aliment in a sipping fashion.*

This plan I would combine with the administration of peptoned enemata, or the very simply prepared enema, which I have found very successful, consisting of two ounces of warm milk with one ounce of cod-liver oil, mingled by shaking in a bottle. I feel sure, from my experience, that lives may be prolonged and crises tided over by such supplementary alimentation.

The foregoing is a brief sketch of the most important agents now at our disposal for restoring the

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* "Lumleian Lectures:" *cf. British Medical Journal,* May 8, 1880, p. 684.

power of the heart-muscle and inducing the compensation in mitral regurgitation occasioned by rheumatic endocarditis, when failure threatens. The restoration of such compensation may not, however, be the only indication. Accidents of the disease, so closely related therewith as to force the necessity of considering them in any question of prognosis and treatment, demand consideration. Such epiphenomena are renewed attacks of endocarditis, pericarditis (especially when accompanied by myocarditis and adhesions), and embolism. These subjects, however, being equally manifest in mitral stenosis and mitral regurgitation, may be conveniently postponed.

8. *General Hygiène and Dietary.*—We may consider this question in its relation to three stages of the affection.

First, in the stage of *complete compensation.* It is by no means uncommon for an individual who is the subject of mitral regurgitation to manifest signs of perfect health. He is ignorant of the fact that he presents any condition of organic deviation from the normal until the truth is brought home to him in an unwelcome manner. It may be that he presents himself to the medical officer of a Life Assurance Company, or he undergoes the medical examination necessary for candidates for positions in the Public Services: then a systolic murmur at the apex of the heart is detected, there is a failure to pass the examination, inquiries are probably made, and to his discomfiture and distress, perhaps, the candidate is informed that he has a crippled heart. I must not stay to argue that cruel injustice is thus often done; the person, to all intents at the time in good health, is not only refused

a career, but is turned into an invalid. It seems to me that the prognosis in such cases of perfectly compensated mitral regurgitation turns less upon the existing valvular lesion than upon the proclivity to rheumatism. A young man who has never suffered rheumatic fever, and who has not manifested any signs of rheumatism from puberty to manhood, has little to fear from a well-compensated mitral insufficiency. On the other hand, there are grave fears if rheumatic symptoms tend to recur.

What are the rules that should be given to the subject of mitral regurgitation who presents no sign whatever of ill compensation? Shall he refrain from exercise and from everything approaching athleticism? The answer, I take it, should be—Certainly not. Let him educate and exercise his voluntary muscles and join in invigorating sports, with the single exception that he shall not participate in severe contests for supremacy. A violent and sudden muscular effort may cause rupture of the already imperfect valve, and a downward course may be at once initiated. Fairly sustained muscular effort will tend to keep the central organ of circulation in good and sufficient tone,

In such cases of well-compensated mitral regurgitation, too, in my opinion the morning cold bath is by no means to be prohibited; there are few agents of greater value as a tonic to the heart.

Unless there are distinct errors in the daily dietary, the latter should be very much after the discovery of mitral regurgitation that it was before it; only decided moderation as regards the use of alcohol should be inculcated.

We will now assume that the case presents itself in the *second* stage—of *commencing failure of com-*

pensation. There are probably some signs of dyspnœa, or, perhaps, commencing dropsy of the feet. In such cases, of course, prognosis is much more grave, and there can be no question that a person presenting any such sign could not legitimately pass successfully through any examination like that I have mentioned. In such a case, is the policy to be one of the most perfect muscular rest attainable? For long it has been the generally adopted plan to keep the patients in bed for a time, and considerably to restrict their movements, but Oertel* has revolutionized this system. He advocates the promotion of vigorous efforts of the cardiac muscle by severe muscular exercise, especially mountain-climbing. So the muscle is made to tend towards hypertrophy; there is a reflex relaxation of the muscular coat of the arteries—an effect said to be much more marked in the case of climbing than in the case of muscular exertion on the level; but the loss of arterial tone is compensated by the enhanced amount of blood driven out of the arteries by the stimulated ventricle, and the velocity of the blood-current is increased. Moreover, the respiratory efforts being stimulated there is acceleration of the pulmonic circulation, and thus oxygenation of the blood is promoted.

Another point insisted on by Oertel in the general management and treatment of these cases, is that the ingestion of water shall be reduced and its excretion augmented. In his cases only 34 to 36 ounces of water, including that contained in the solid food, were allowed *per diem.* It is better to obtain the increased

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* "Handbuch der Allgemeinen Therapie der Kreislaufs Störungen:" *Ziemssen's Cyclopedia.* 1884.

elimination of water by the way of the skin than by the way of the kidneys. The climbing exertion tends to promote free diaphoresis. This may also be accomplished by Turkish baths, or by the administration of pilocarpine.

The diet should be so ordered as to minister to the muscular tissues and to diminish the fat. The best proportions of food are said to be not more than about one ounce of fat, three and a quarter ounces of carbohydrates, and not less than five ounces of proteids. When improvement is manifested, and the circulatory balance is restored, the amount of fluid in the daily food should continue to be restricted. A cup of tea may be taken morning and evening; about half a pint of claret, from eight and a half ounces to rather more than a pint of water and a little over three ounces of soup, should constitute, besides that contained in the solids, all the fluid taken during each day. The solid diet should be rich in nitrogen—*e.g.*, bread four to five ounces, meat or fish six to seven ounces, with chicken or game five ounces, one or two eggs, a little salad, cheese, &c., and three and a half to seven ounces of fresh or cooked fruit.

The points advanced by Oertel are no doubt of high importance, but the rigid application of his plan in all cases of commencing heart-failure would be much to be deprecated. In the early stages of failure of compensation, the coddling plan whereby the heart-muscle is kept at a minimum exercise of function is, as I have before said, contrary to sound physiology and to good practice. Graduated exercises, judiciously increasing calls upon the heart-muscle whereby its functional activity is promoted, are indicated. It may not be desirable for the patient to seek for rest

at the earliest moment of distress, yet he should hasten slowly. The task which he cannot accomplish to-day he may easily fulfil to-morrow. It is difficult to subscribe to the doctrine that it is necessary that the exercise should be in the nature of ascending heights, and the prescription to a dweller in cities that he should periodically go up and down stairs may scarcely be taken *au sérieux*. It is quite legitimate, however, and may be sufficient, to urge that the patient shall walk rather than ride, and shall walk systematically; and that if he ride for a certain distance he shall descend from his carriage at intervals and do a spell of muscular exercise. I can readily subscribe to the doctrine that a free action of the sweat-glands is also a valuable end to attain: but to force exercise until this is attained in full degree may not be desirable. A method of treatment which, I consider, can be strongly recommended to promote such diaphoresis—one which can be combined with that of graduated muscular exercise—is *Massage*. If once or twice a day the limbs and body are shampooed with hot water the peripheral circulation—languid from the failing circulatory power—is quickened, elimination is promoted, and much good results.

I am in favour of Oertel's plan, with certain restrictions; but there must be a selection of cases. As I have said, in uncomplicated instances of failure of compensation in mitral regurgitation, in the gouty, in obese subjects, in those in whom fatty changes are probable, and in anæmic subjects, the plan is good, whilst the policy of rest is hurtful; but it is not easy always to determine whether the cases are or are not complicated. If a slow endocarditis be in progress, the method is unscientific and unsafe; in all cases,

therefore, it should be put in force with caution and with careful estimation of the cardiac conditions, and of the effect of exercise upon them.

My own experience is distinctly in favour of *massage* as an adjunct to the treatment of cardiac disease when compensation begins to fail. It may be asked whether favourable results have been attained in any of the continental water-cure establishments, where this system has been brought to a high state of efficiency; and concerning this question important evidence has lately been brought forward by Dr. Blanc of Aix-les-Bains.* The sending patients suffering from diseases of the heart to thermal health-resorts, where the chief plan of treatment is the application of hot water to the surface of the body, has generally been discouraged. No doubt the proximate reason is that the immediate result of the treatment has been the favouring the efflux to the capillaries, and therefore an increase of the violence and frequency of the cardiac pulsations. Symptoms of distress, therefore, were early manifested, and the patient and those upon whom his care devolved were discouraged. Dr. Blanc, however, produces evidence which shows that the objections must be reconsidered, and that good results may attend a perseverance with the treatment. The system adopted at Aix-les-Bains provides that the hot water, which is projected by means of the douche upon the patient, can be regulated, and must always be of uniform pressure and temperature. By a special arrangement

* "Des Affections Cardiaques d'origine rhumatismale traitées aux Eaux d'Aix-les-Bains" (Savoie), par le Docteur L. Blanc, Medecin-Inspecteur aux Eaux d'Aix, &c. Paris and Aix-les-Bains. 1886.

the water that is distributed over the chest and upper extremities comes with less force than that which is directed on the lower limbs—the distribution is effected in an agreeable manner, and absolutely without shock. Moreover, skilled massage is practised at the moment that the water is projected upon the surface. By a merely mechanical process, therefore, the peripheral circulation is quickened, the suppleness of the joints and of the muscles is increased, and the excretions are promoted; in fact, as Dr. Blanc says, an artificial exercise is induced to replace the exercise of normal movement from which the victim of heart-disease or rheumatism, and especially of both combined, is debarred. The temperature of the water employed is about 90° Fahr. (varying between 32° and 34° Centigrade); the usual duration of a douche is ten to fifteen minutes, but this may be reduced to eight or five minutes in special cases; the douche is generally given daily for three days, then there is one day's interval. The first effect of the douche is a slight quickening of the pulse, but when the patient reposes after the bath this acceleration passes off, and frequently the rate becomes slower by five or six pulsations. The ordinary treatment after the bath at Aix-les-Bains, in the case of a rheumatic patient, is to apply one or more coverings, termed the *maillot*, for twenty or thirty minutes to obtain free diaphoresis. This is not done, however, in the case of a patient with heart-disease, when a simple flannel robe only is to be worn, and a repose of at least an hour is enjoined. Amelioration of the heart-symptoms is not at once attained; in articular rheumatism the suffering under the treatment at Aix-les-Bains is at first aggravated—a like result seems to attend as regards the cardiac phenomena; there is an

increase in the pronunciation of the cardiac murmurs already existing; whilst murmurs due to vascular and hæmic causes disappear, organic *bruits* are at first intensified. As treatment progresses, however, and generally after a week, there is sensible improvement, and the engorgement of viscera, the consequence of the cardiac lesion, diminishes and disappears. Dr. Blanc adduces very important evidence to show that not only is compensation quite restored, but the endocardial inflammation with its results of plastic effusion may disappear and leave no trace.* Of fifty-two cases of mitral regurgitation, Dr. Blanc records fifteen in which all signs of the condition of disease passed away under the treatment, whilst twenty-one manifested improvement and sixteen were stationary. Details are given of many of these cases which indicate that, though there were pronounced physical signs of the valvular lesion with the usual phenomena of ill-compensation following them, there was not only a disappearance of all the cardiac troubles, but a complete vanishing, confirmed by repeated examinations, of the murmurs. I need not here debate the question whether all the murmurs observed were due

* "L'expérience m'a démontré qu'à cette amélioration générale pouvait se joindre une amélioration locale, qui, dans certains cas, allait jusqu'à la guérison. Sous l'influence de cette congestion passagére de l'endocarde, ou de toute autre cause qu'il est difficile d'apprécier, les dépôts plastiques qui s'étaient formés sur les valvules se résorbent et de là ces guérisons dont je vais dans un instant citer plusieurs observations. Ces guérisons ne peuvent survenir, comme on e comprend bien, que quand la lésion est de date récente, qu'elle succéde à une attaque de rhumatisme aigu ou subaigu, et de là l'indication d'envoyer les malades à une période assez rapprochée de la maladie, productive de la lésion." —*Loc. cit.* p. 19.

to actual physical changes in the endocardium. It is sometimes difficult, it may be impossible, to distinguish between a murmur due to structural change of the valve and one due to exocardial causes. Moreover, a murmur of mitral regurgitation may be due, as I have before argued, to mal-apposition of the valve-curtains, owing to feebleness of the ventricular muscle or to inflammatory changes amongst its fibres. I have myself, however, had evidence that a murmur having all the characters of that produced by fibrinous exudation from the endocardium—a murmur of great intensity, and having the most pronounced musical character—*may* disappear and leave no trace whatever. Dr. Blanc makes out a strong case for the treatment of rheumatic endocarditis by the method, or some modification of it, pursued at Aix-les-Bains, and his results encourage my belief that in well-conducted *massage* we have a valuable adjunct to treatment.

LECTURE III.

MITRAL STENOSIS.

Morbid Anatomy—Physical Signs—Differentiation from the Lesion which induces Regurgitation—Rise and Progress of the Disease resulting in Stenosis—Compensation—Special Treatment in Mitral Stenosis—Objections to Digitalis—Convallaria majalis—Analysis of Cases treated—Caffeine, &c.—Conclusions—Complications of Mitral Disease—Pericardial Adhesions—Embolism.

I PROPOSE now to consider the morbid conditions associated with a structural change at the left auriculo-ventricular aperture—a change which narrows this outlet and impedes the influx of blood into the left ventricle during the period of diastole. No disorder of function can bring about such a condition as this; the lesions are always organic.

We will first glance at the *morbid anatomy* of the affection. If the mitral aperture be viewed from the auricle it may, in many cases, be seen that a smooth septum presents itself between auricle and ventricle, crossed by a narrow slit, almost straight, but inclining to be crescentic. Such slit may be no larger than that a sixpenny-piece or a shirt-button will pass through, and from its appearance the orifice has been termed the "button-hole mitral." The natural form of the curtains may be entirely lost, their place being occupied by a thick fibrous structure welded at its circumferential attachment with the cords and fleshy columns, which may all be transformed into a dense tendinous

mass. In certain cases this fibrous material is infiltrated with calcareous salts to such a degree as to make it closely resemble bone.

Another, but less frequent, form of obstruction is that in which the mitral orifice, as seen from the auricle, resembles a hollow cone. This is known as the "funnel-mitral." Its ventricular outlet may be so small that it will scarcely admit the point of the little finger. Dr. Hilton Fagge has recorded forty-six examples of the button-hole to one of the funnel form of constriction; Dr. Hayden, thirteen of the former to one of the latter; and of my own records of twenty autopsies in cases of mitral stenosis, two only were "funnel-mitral." M. Lancereaux has described a case of mitral stenosis in which, amongst the vegetations which surrounded the thickened orifice, he discovered hard granules, that were shown by chemical tests to consist of urates. When heated with nitric acid they gave rise to a yellowish product (alloxan), and this, on the addition of ammonia and distilled water, gave the characteristic red colour of murexide or purpurate of ammonia. The granules, when dissolved in acetic acid, crystallized in the characteristic rhomboids of uric acid.* I draw attention to this observation because it may have an important bearing on the questions of etiology and treatment. I have myself met with a case of mitral stenosis in which there were abundant gouty deposits in the joints, some of which suppurated, and gave exit to uratic concretions intermixed with the pus.

In rare cases—Dr. Byrom Bramwell has observed

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* "Anatomie Pathologique," p. 215. Paris: Victor Masson Fils. 1871.

three such—the mitral segments are quite healthy and the stenosis is due to the presence of large calcareous nodules in the muscular wall of the ventricle. These nodules may be associated with atheroma, may consist of urates, or may represent syphilitic gummata which have become calcified.*

Dr. Bedford Fenwick has collected a large number of cases of stenosis of the tricuspid valve, and the important lesson is taught by these that the lesion is nearly invariably accompanied by stenosis of the mitral. Dr. Wilks points out that in these the narrowing of the mitral orifice is secondary upon that of the tricuspid, for in primary obstruction of the tricuspid, which allows only a small quantity of blood to pass into the right ventricle and lungs, "a diminished supply is sent to the left heart, and in this way its cavities with its orifices would be reduced in size."† It is thus rendered very probable that in some cases of mitral stenosis the cause is twofold—in part inflammatory from endocarditis, and in part developmental.

It is obvious that the great difficulty created by such alterations as these is the due filling of the ventricle from the auricle. In addition, there is, however, in many cases necessarily a reflux into the auricle at the systole of the ventricle. In proportion as the slit is narrow the possibility of such reflux is less, and in extreme cases of stenosis it appears probable that no regurgitation is possible. In all

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* "Diseases of the Heart and Thoracic Aorta," by Byrom Bramwell, M.D., F.L.C.P.E. Edinburgh: Young J. Pentland. 1884.

† *Lancet*, Jan. 2, 1886, p. 7.

cases the main difficulty is the obstruction; that of regurgitation is subsidiary, though frequently co-existent.

It requires only a slight consideration to be convinced that quite a different set of conditions obtains in mitral stenosis from that manifest in mitral regurgitation. Morbid anatomy teaches us that in stenosis the left ventricle is usually not dilated; it has its normal capacity, or is even smaller than natural. We should expect so, for the difficulty is not that the ventricle is habitually overfilled as in regurgitation, but that it is insufficiently supplied owing to the imposed obstruction. When the left ventricle is observed to be dilated in the autopsy of a subject of mitral stenosis, it is probable that mitral regurgitation or disease of the aortic valves conduced to such a change. Upon the left auricle the consequences of mitral stenosis are very manifest. It is usually not only dilated, but hypertrophied. The wall of the auricle may be increased in thickness from its normal of about three-twentieths of an inch (Bouillaud) to a quarter of an inch or more. I have found it a quarter of an inch thick in a case of mitral stenosis in a child. On the other hand, it is occasionally found dilated rather than hypertrophied. In one case I found it extremely dilated, and the walls almost as thin as an ordinary visiting-card. The dilatation and hypertrophy of the left auricle are also in accord with *à priori* considerations, for the cavity becomes overfilled on account of the obstruction to its outflow, and the muscle has a heavier task than the normal in aiding the filling of the ventricle. When dilatation is in excess, it is through an unusual failure of muscular power.

I turn now from the morbid anatomy to the *clinical history* of mitral stenosis, and I shall have to crave your indulgence if I seem to dwell too long upon points which may not appear at first sight to have a very distinct bearing upon treatment. I feel sure that I shall have your concurrence when I say that no disease is well treated that is misunderstood. We have a great deal to learn as to mitral stenosis; it is, I feel quite sure, in many instances, unrecognised—not from any fault in observers, but from their misfortune. It is only comparatively recently that our pupils could be taught in our hospitals the methods of discriminating between cases of mitral stenosis and those of mitral regurgitation, and it is unwise to conceal the fact that difficulties in such differential diagnosis do occur. But it has, to my mind, been too hastily assumed that the consecutive changes and collateral phenomena in the two conditions are so closely similar that a plan of treatment for the one is equally applicable to the other. I need not ask you to concur with me in deprecating the plea of *Cui bono?* It is our bounden duty to learn all we can of the disorder we have to treat, even if the immediate influence of such knowledge upon treatment be not so very apparent.

Let us consider the signs by which we may recognise the condition of mitral stenosis. 1. *The murmur.* This is heard in the neighbourhood of the apex of the heart, in the mitral area, but, according to my experience, usually rather to the right of the apex. It occupies the diastolic period—the long pause—usually the concluding portion of it, and then it terminates abruptly with the first sound. It is chiefly Dr. Fauvel of Paris, and Professor Gairdner of

Glasgow, we have to thank for accurately describing this murmur and making it available for the practical purposes of diagnosis. The distinction between the murmur indicating mitral stenosis and that indicating mitral regurgitation is to be made partly by the character of the sound and partly by the rhythm. The stenosis-murmur is usually of a rattling and rolling character, but its chief characteristic is its abrupt termination—it ends with a sudden stop, as the murmur of regurgitation *never* does. Even when the murmurs of stenosis and regurgitation are combined there is usually a spot in the neighbourhood of the apex at which the former is heard to stop suddenly, and the systolic murmur to "tail-off" from it. The rhythm is determinable by ascertaining the relation to the second sound and to the impulse of the heart. In approaching the apex from the base one may be convinced of the commencement of the murmur after the second sound. Near the apex one may hear that the termination of the murmur is with the impulse of the heart as felt upon the chest-wall, or, where this cannot be determined, with the pulsation of the carotid in the neck. Such are, very briefly, the chief characters of the murmur which is so commonly known as the *presystolic* murmur that has been considered to be almost, if not absolutely, pathognomonic of mitral stenosis. And now as to its mode of production—a question which is really of practical importance. Some observers have considered it due to the muscular contraction of the auricle urging the blood through the stenosed aperture into the ventricle. It is well known that Professor Gairdner proposed the term "auricular-systolic" to denote the murmur, but he did not ascribe its production wholly to the

muscular contraction of the auricle. Dr. Wilks* considered that the murmur might anticipate the auricular systole, that it might occur "not only during the contraction of the auricle, but also during the heart's diastole and pause." Dr. Galabin came to a like conclusion from the evidence afforded by the cardiograph. I am able to afford the crucial proof of the view that the causation of the presystolic murmur may be independent of the auricle: *first*, because in many cases I have observed that though there has been present a prolonged presystolic murmur com-

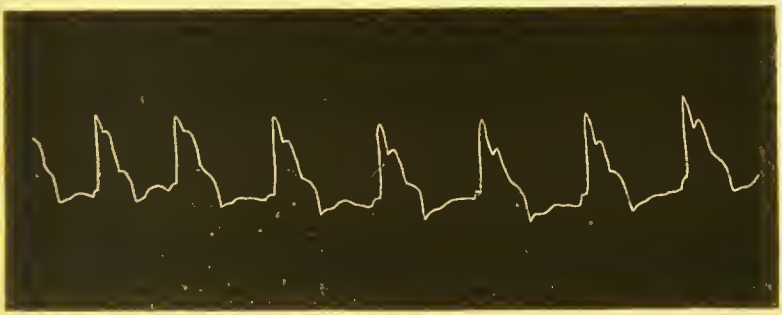

FIG. 15.—Cardiogram from a case of mitral stenosis with presystolic thrill and murmur, showing the auricular systole in the normal position.

mencing in the long pause almost immediately after the second sound, cardiographic evidence has shown the auricular systole to occupy its normal position just anterior to the commencing contraction of the ventricles (Fig 15);† *secondly*, because I observed a case in which a murmur occupied at one time a portion of, and at another almost the whole of, the long pause; and the autopsy showed that the auri-

* *Guy's Hospital Reports*, third series, vol. xvi., March 1871.

† "Manual of the Physical Diagnosis of Diseases of the Heart," third edition, p. 278. London: J. & A. Churchill. 1881.

cular systole could have had no share in producing such murmur—for not only was the left auricle so dilated that its wall could have exerted no appreciable muscular power, but it was lined by a closely adherent old laminated blood-clot. I consider that it is clearly proven that the so-called presystolic murmur may occur during the diastolic as well as the presystolic period, and that it may be due to the entrance of blood into the ventricle directly diastolic relaxation permits, the blood being urged through the stenosed aperture owing to the tension under which it has been retained in the elastic and distended auricle and the pulmonary veins. The contraction of the auricle may reinforce the murmur and make it loudest just before the ventricular contraction. This consideration explains why, in exceptional cases, the murmur of mitral stenosis is post-diastolic and ceases with a distinct pause before the first sound, the auricular systole in such cases being weak or imperfect (Fig. 16). It is certain that in a large majority of instances the presystolic murmur serves to indicate with precision the existence of mitral stenosis. The late Dr. Hayden has said: "It is *never* present where mitral narrowing does not exist, and it is never absent, and that only for a very limited period, in cases of that lesion."* I am sorry that I cannot concur in so positive a statement. In a few cases I have found the presystolic murmur closely simulated by the murmur of aortic regurgitation, when this is conducted towards the apex, and especially, as is sometimes the case, when it is heard *only* in the mitral area. Cases have been recorded in which a presystolic murmur has

* "Diseases of Heart and Aorta," p. 898.

been noted during life, and the autopsy has demonstrated not mitral stenosis, but aortic regurgitation. Another possible source of error is the existence of pericarditis, when friction may be occasioned by the auricle, and cease at the moment of systole. Again, I think, most observers will agree that in some cases the presystolic murmur is extremely variable : it may be inaudible during repose, and yet very evident when the patient is made to manifest some slight exertion ;

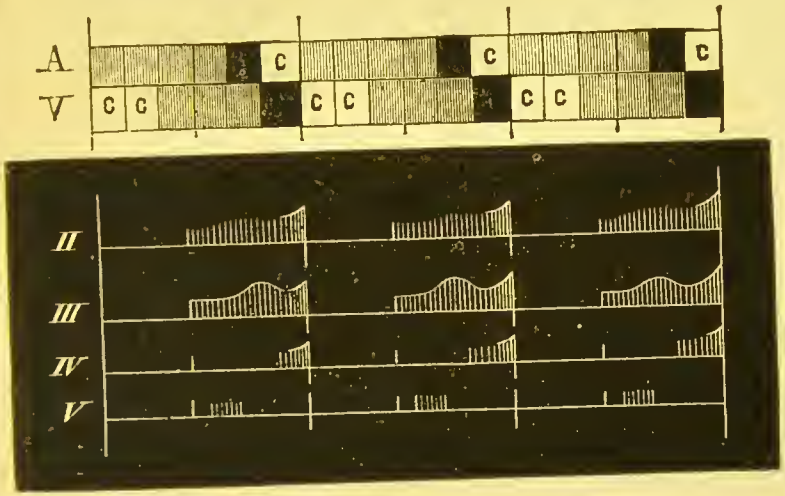

FIG. 16.—Diagram illustrating various forms of the murmur indicating mitral stenosis. II. Prolonged murmur from second to first sound. III. The same with reinforcement during its progress. IV. Presystolic murmur with reinforcement at its close. V. Post-diastolic murmur. A and V indicate the coincident phenomena in auricle and ventricle, the dark squares the periods of filling. C C, the systole or contraction.

it may be absent for considerable periods, and then be readily discoverable. Although, therefore, I consider that in the great majority of cases the presystolic murmur declares with precision the existence of mitral stenosis, it is necessary to consider other signs before committing oneself to a positive opinion.

Another auscultatory sign of great importance in indicating the obstructive lesion is (2) *reduplication, or a seeming reduplication, of the second sound of the heart.* This phenomenon is to be noted in at least a third of the cases of mitral stenosis, and only rarely in other

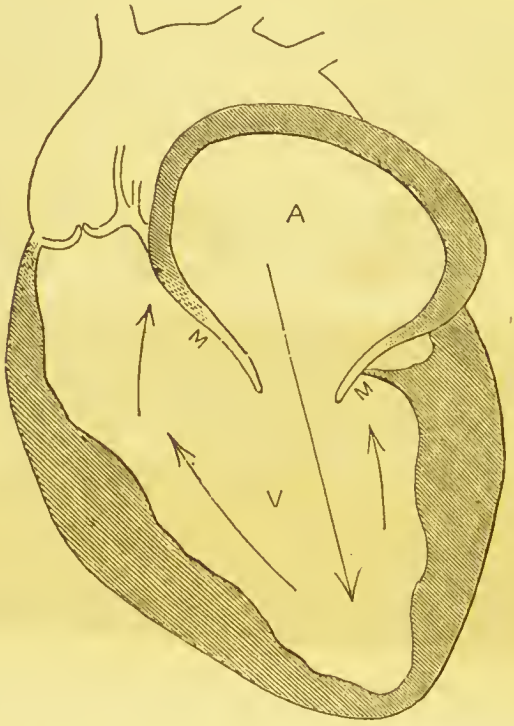

FIG. 17.—Diagram illustrating mechanism of pseudo-reduplication of heart sounds. Ideal section of left auricle and ventricle. M, M, curtains of mitral valve; the arrows show the direction of the flow of blood in diastole and auricular systole.

conditions. It becomes, therefore, a valuable aid to diagnosis. I have formerly developed before the Society at length my views as to the mode of production of this seeming reduplication.* I will only

* *Proceedings of the Medical Society of London*, vol. v. p. 191.

say here that I believe it to be due not to any want of synchronism in the closure of the aortic and the pulmonary semilunar valves, but to the normal second sound followed by another sound due to a sudden tension of the mitral valve itself. The blood, accumulated under pressure in the auricle, rushes through the stenosed aperture as soon as diastolic relaxation permits, and jerks the mitral curtains or the thickened material which represents them on the ventricular aspect (Fig. 17); this gives rise to a sound of tension, which, coming closely after the normal second sound, appears like a reduplication of the latter (Fig. 18). The great anterior flap of the

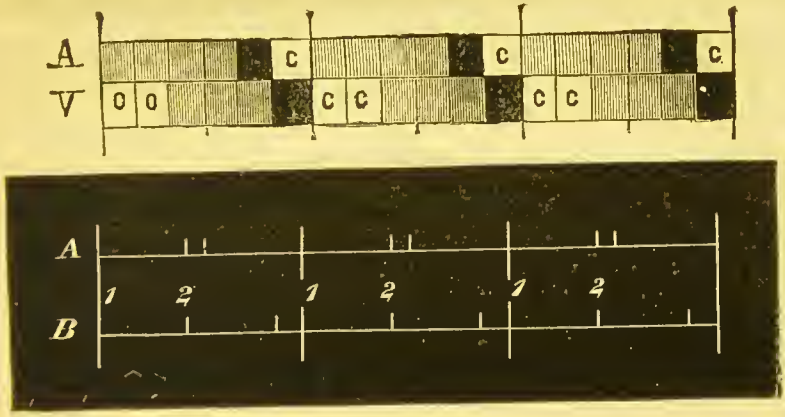

FIG. 18.—Diagram illustrating positions in cardiac rhythm of pseudo-reduplications of heart-sounds. A, presystolic tension of mitral curtains occurring early, pseudo-reduplication of *second* sound. B, tension occurring late, pseudo-reduplication of *first* sound.

mitral valve is normally on the stretch in diastole; in Dr. MacAlister's words, "it does not hang loosely down, it is stretched taut from basal ring to muscle tip."* It does not seem difficult to realize that in

* *British Medical Journal*, Oct. 28, 1882, p. 825.

the condition of stenosis, and for the reasons given, this diastolic tension may be so increased as to give rise to sound (Figs. 19, 20).

A third sign of importance in establishing the diagnosis of mitral constriction is (3) *thrill*. A thrill at the apex is rarely met with in mitral regurgitation, but very commonly in mitral stenosis. Its rhythm

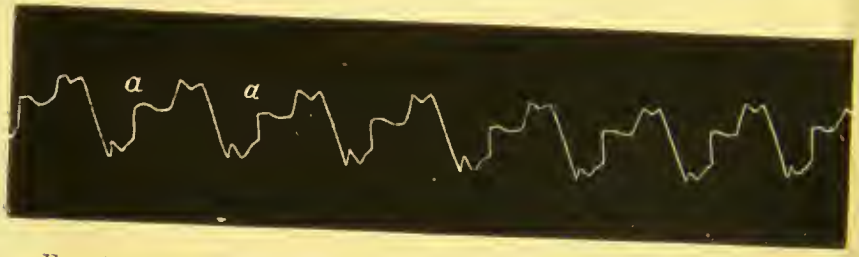

FIG. 19.—Cardiogram in mitral stenosis with pseudo-reduplication of second sound. The eminence *a*, indicating the systole of the auricle, is greatly exaggerated.

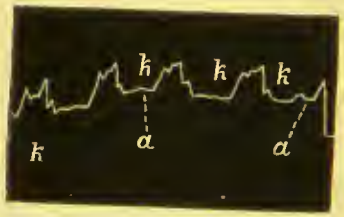

FIG. 20.—Cardiogram in pseudo-reduplication of second sound. Eminence *k* due to diastolic closure of semilunar valves is followed by an eminence *a*, indicating rise of blood-pressure in the diastolic portion.

is determinable in like manner with that of the murmur, and if it be presystolic the diagnosis of mitral constriction is assured. I have observed presystolic thrill when there has been no presystolic murmur, and where the condition of stenosis has been indicated by other signs.

A fourth means of differentiation is (4) *the deter-*

mination by percussion of the outline of the heart. If this be done accurately by means of a pleximeter, and marked upon the chest-wall with a copying pencil, a transfer may readily be taken upon paper and kept for reference. By this method I have shown in some cases—(1) an abnormal bulging in the situation of the left auricle ; (2) a dilatation of the right cavities and of the pulmonary artery, with an absence of dilatation of the left ventricle. The concurrence of

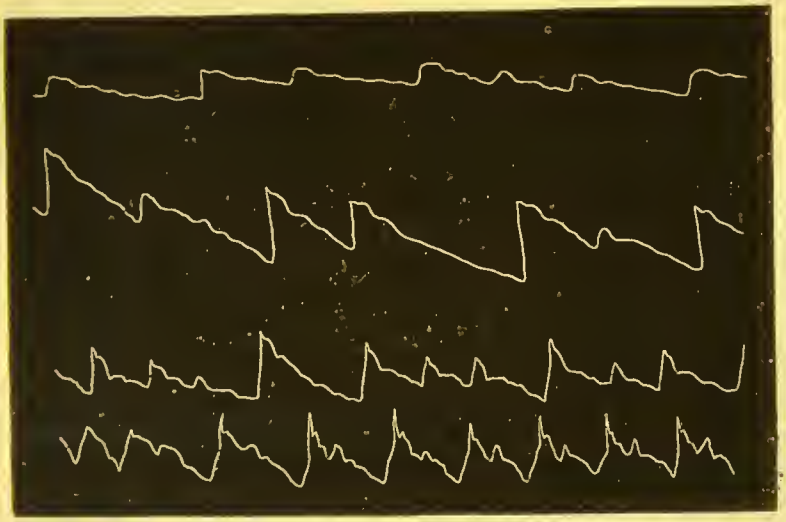

FIG. 21.—Sphygmograms in mitral stenosis showing interpolated systoles.

these signs has strongly suggested the diagnosis of mitral stenosis when other signs have been obscure.

Lastly (5), a valuable aid to diagnosis may be received from the *employment of the sphygmograph and cardiograph.*

Very contradictory opinions have been put forth as to the pulse of mitral stenosis. Dr. Hayden considered that "the pulse of mitral obstruction is usually quite regular, not above ninety in the minute,

but small,"—that is, until the later stages, when failure commenced; and Dr. Fagge thought that in the majority of cases in which a presystolic murmur was heard the pulse gave no indication of the existence of disease. A large number of observers, however, have noted irregularity of the pulse as pertaining to mitral constriction.* My own observations point strongly to a notable irregularity of the pulse in mitral stenosis; and this in such degree as to afford valuable diagnostic evidence. In mitral regurgitation the pulse is usually regular until compensation is beginning to be imperfect and the right chambers commence to yield. In mitral stenosis, however, irregularity may be evident when compensation is perfect. It is true that many observations may be made with a record only of an even and regular pulse; but with repeated observations the peculiarity of mitral stenosis becomes manifest in the trace—a double or even triple pulse is recorded before the base line of the sphygmographic trace is reached (Fig. 21). These pulsations are due to repeated systoles, the normal correlation between auricle and ventricle being disturbed. In the later stages, when the right side of the heart commences to fail, irregularities in volume of the pulse may be observed; and in a case where there was great dilatation of the auricle, I found the pulse become extremely slow, its rate falling from eighty to fifty-six, and then to an average of forty per minute. At one time it was thirty-six.

The evidence afforded by the cardiograph, when mitral stenosis is suspected, is, in my opinion, ex-

* See list in Balfour's "Clinical Lectures on Diseases of the Heart," second edition, p. 123. London: J. & A. Churchill. 1882.

tremely valuable. The trace enables one to judge of the relative length of systole and diastole. In free mitral regurgitation a very short interval separates the systoles; the duration of the systole, instead of being, as in the normal, less than that of the diastole, is greater. In stenosis, on the other hand, the interval between the systoles may be greatly prolonged; or in stenosis the diastolic intervals may be observed to vary greatly in duration. Two systoles may occur with no appreciable diastolic interval, and another interval may be abnormally protracted. Much more characteristic, however, is the appearance of a number of vibrations in the diastolic part of the trace; in fact, the vibrations which are heard by the ear as murmur, or felt by the finger as thrill, may be written on the smoked paper by the needle of the cardiograph. I show you many examples. In some it will be seen that the diastolic portion is serrated, and there is no indication of the elevation caused by the auricular systole just before the main upstroke indicating the grasp of the ventricle; in others vibrations are seen to precede a defined systole of the auricle; in a third set the auricular systole is well marked, and the sonorous vibrations of murmur, though murmur existed, are not recorded. So I think we have a means of determining in some measure the degree of constriction. If such were considerable it is unlikely that the auricular systole would be readily transmitted and recorded; on the other hand, it is likely that the finely serrated line of vibrations would be produced by the extrusion of blood through the narrowed aperture.* Some of my

* In some instances there is cardiographic evidence of two or even three auricular systoles in one diastolic period.

tracings show in a marked manner the effect of effort in rendering evident vibrations in the diastolic portion which were not visible during repose. By a comparison, too, of the characters of the systolic and diastolic portions I think we are enabled to obtain some indications whether, in combined stenosis and regurgitation, the former predominates over the latter or otherwise, and whether or no hypertrophy preponderates over dilatation of the ventricle (Figs. 22, 23, 24).

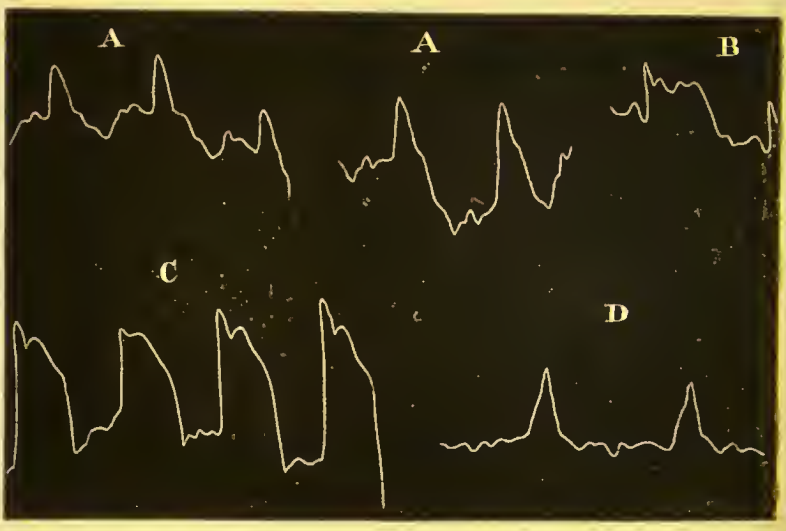

FIG. 22.—Cardiograms in mitral stenosis. A A, eminences indicating high blood-pressure in diastolic period. B, pronounced auricular systole. C, D, irregular undulations and serrations in diastolic period.

Such are the chief means at our command for arriving at a diagnosis of mitral constriction; and, though I do not think we are justified in coming to a conclusion from observation of the sign alone, I consider that, by a judicious combination of methods of observation, no case of mitral stenosis ought to go unrecognised.

I pass on now to consider the clinical evidence as to the *origin and course of the morbid changes which bring about the obstructive lesion.* We are at once met by a body of evidence which shows that mitral

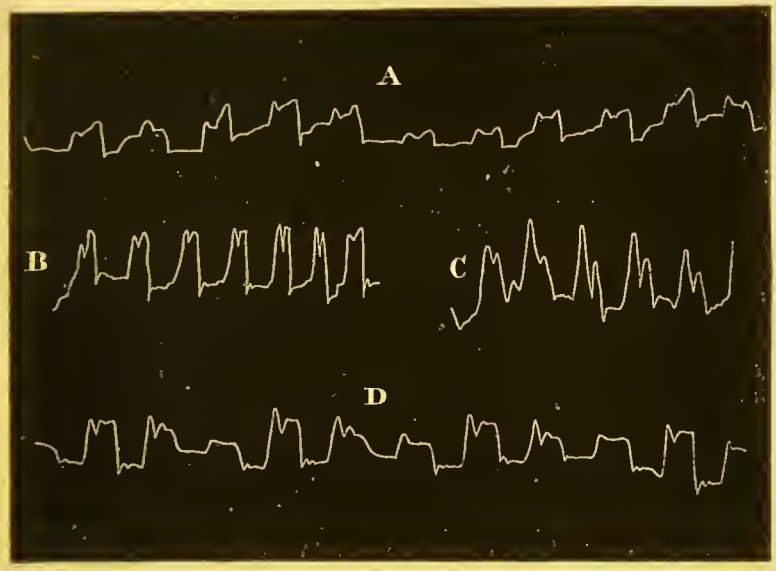

FIG. 23.—Cardiograms in mitral stenosis.

FIG. 24.—Cardiogram in mitral stenosis showing vibrations in diastolic period corresponding to presystolic murmur and thrill.

stenosis, like mitral regurgitation, has a strong relationship with rheumatism. From the morbid anatomy standpoint it has been supposed that, at least in some cases, the lesion might have been congenital. The smooth surface of the septum between

auricle and ventricle, with its symmetrically edged aperture, might *primâ facie* support this view; but we do not find the lesion commonly associated with those which are undoubtedly congenital; and these are, moreover, infrequent in the left, though comparatively frequent in the right chambers of the heart. In one of the twenty post-mortems, however, which I have recorded, a large permanent foramen ovale was present, the subject being a female aged fifty. It is known that such congenital disease, as Dr. Peacock formerly pointed out, predisposes to endocarditis, and it is probable that such was the sequence in this case; for we are met by many observations which show that the lesions of stenosis, which in appearance suggest a congenital causation, are met with in cases which are undoubtedly rheumatic.

Sir Dyce Duckworth has collated the records of 264 cases of mitral stenosis from various sources, including eighty observed by himself, and the figures show that 141, or 60·8 per cent., manifested in some form rheumatic antecedents. Of sixty-four cases observed by myself, and of which I have records, exactly thirty-two (50 per cent.) had been the subjects of rheumatic fever, subacute rheumatism, or rheumatoid pains. The association, therefore, of mitral stenosis with rheumatism is an intimate one. When we come to inquire, however, as to the degree of such association comparatively with that subsisting between mitral regurgitation and rheumatism, I think we shall find the relationship less marked in the one case than in the other, and I hope that the inquiry will not be unfruitful as regards the determination of the nature of the change which induces mitral stenosis. If I take the cases of mitral regurgitation derived

from the same sources (viz., private and hospital practice) from which I obtained the cases of mitral stenosis that I have mentioned, I find that of 123 cases, seventy-three, or 59 per cent., presented evidence of rheumatism in their history. But it must be recollected that in a considerable number of the cases of regurgitation organic disease was not present or not proved, whilst mitral stenosis is always due to organic change. It follows that the figures do not sufficiently express the relation between rheumatism and the organic change which induces *regurgitation* at the mitral orifice. From the analysis of cases of cardiac disease prepared from the records of the London Hospital by Dr. Gabbett for the year 1880, it will be found that whilst 58 per cent. only of the cases of mitral stenosis presented a history of rheumatism, 77 per cent. of the cases of mitral regurgitation were rheumatic.

And now, to push this question further, let us inquire as to the *degree* of manifestation of rheumatism in the two classes of cases. First, as to the relation with acute rheumatism. If we examine the records of acute rheumatism in the London Hospital for 1880 and 1881, we find that the proportions of cases of mitral stenosis (including those in which stenosis was combined with regurgitation) stand thus:—Proportion to all cases in a first attack of acute rheumatism, 5·6 per cent.; in patients suffering a second attack, 3 per cent.; in those with a history of two or more previous attacks, 1·7 per cent. It is obvious that this relationship differs very widely from that existing between mitral *regurgitation* and acute rheumatism, where the proclivity to the lesion increases with the attacks. It is obvious, therefore, that a close relation does not

obtain between mitral stenosis and the acute forms of rheumatism, and that repeated attacks do *not* generally tend to produce the lesion.

As a further step towards the elucidation of the question, I will now ask you to follow me in the inquiry as to the etiology of mitral stenosis in the cases of children. I think you will agree with me that a considerable light can be thrown on the subject from this source. Contradictory opinions have been enunciated as to the proclivity of children to the affection. Dr. Hayden thought that it was to be met with most frequently in children; while Dr. Fagge had no patients under ten, and the youngest observed by Sir Dyce Duckworth was fourteen. The cases I shall now call your attention to were all under twelve years of age; I have had many who were under seven years old. I have tabulated these cases according to the degree of manifestation of rheumatic symptoms. In those who suffered from *acute rheumatism* I found twenty-four cases of mitral regurgitation to one of mitral stenosis; in those classed as *subacute rheumatism*, thirteen of mitral regurgitation to two of mitral stenosis; in those who suffered only *rheumatoid pains*, six of mitral regurgitation to two of mitral stenosis. So far as this evidence goes, therefore, it tends to show that it is not the more severe, but the slighter forms of articular rheumatism, which are attended with the obstructive lesion, whilst the opposite is the case as regards the regurgitation.

To pursue the point, where the rheumatic tendency is not so obvious, but where, as I have said in my first lecture, a rheumatic form of endocarditis is nevertheless manifest, we will consider the cases occurring after scarlatina and measles. In cases

presenting a history of scarlatina I found thirteen cases of mitral regurgitation to two of mitral stenosis; in those with a history of measles, twelve of mitral regurgitation to two of stenosis. Lastly, in the case of children in whom no history of rheumatism was manifest, nor any disease which we might suppose to be likely to induce endocarditis; in these I found twenty-four cases of mitral regurgitation to *fourteen* of mitral stenosis. It is obvious, therefore, that the proclivity to the obstructive lesion is in a very marked manner greatest where articular phenomena are not manifest at all. It might be thought that this was evidence rather against the view that rheumatism is a cause of mitral stenosis; but, as I have shown in my former lecture, the advent of endocarditis having the essential characters of that associated with rheumatism, may be so insidious that no subjective sign marks its onset, and we have found in many instances that the course of the affection in the non-articular examples and the morbid changes, as shown by post-mortem examination in the fatal cases, do not differ in any appreciable way from those which are manifest in cases having a distinct history of rheumatic causation. It would, therefore, appear most probable that the correct conclusion is not that mitral stenosis is independent of rheumatism, but that it is associated with the less pronounced forms of it—with its insidious, and not, so to speak, with its *explosive* varieties.

The arguments adduced by Dr. Wilks are very important, and render it very probable that in some of the cases of mitral stenosis in children the arrest of development of the left chambers with their valvular mechanism plays an important part in the production

of stenosis. In cases where there have been no history of endocarditis, though this probably may have at some time occurred and where the valves may have become contracted without much thickening, the usual secondary effects of hypertrophy of the left auricle and of the right ventricle do not, and need not, occur. Then "it is evident that the whole of the blood of the body coming back to the lungs and then passing again to the left side is measured by the size of the mitral orifice. If this be small, the blood passing through it is diminished in quantity, and it becomes a gauge of the reduced circulation. The left ventricle is therefore small, and the whole heart correspondingly diminished in size. The lungs are small as well as the chest, and the respiratory process correspondingly lowered, and with this probably the whole body is impoverished; at all events the organism is working with a diminished amount of blood."* In such cases the whole economy becomes gradually adapted to the circulatory starvation, and the patient may reach adult life without betraying any symptoms.

And now let us consider the evidence which clinical observation affords us of the mode of onset of the obstructive mitral lesion. I will give, as briefly as possible, some cases illustrative of the various ways in which the clinical signs indicate the disease to arise.

I. *Presystolic Murmur developing insidiously without Signs of Rheumatism.*—A lady (Mrs. M.), aged fifty-two, came under my care in 1876 for dyspepsia with very slight jaundice. She manifested no history of, nor

* Consequences of Narrowing of the Mitral Valve when occurring in Childhood, by Samuel Wilks, M.D., LL.D., F.R.S.: *Lancet*, Jan. 2, 1886, p. 6.

predisposition to, rheumatism. I had frequent opportunities of examining the heart, and there were no signs whatever of lesion. In January, 1877, there having been no symptoms other than an occasional slight dyspepsia previously, the patient complained of "fluttering at the heart," and I found just right of the apex a rough presystolic murmur abruptly terminated by the impulse. I do not think it possible that such sign could have been overlooked in my previous examinations. I can have no doubt that the lesion of stenosis developed gradually without any subjective signs to mark its onset. I have watched the case at intervals ever since; there have been no articular phenomena. The presystolic murmur has been attended with quasi-reduplication of the second sound, and a few months after its first becoming evident a short systolic murmur at the apex was observed also. The systolic murmur increased in intensity, the presystolic continuing to be entirely characteristic. During the whole period until the present there have been no articular troubles, and the cardiac complication, though giving rise occasionally to very slight symptoms, is for the most part, and for long periods, accompanied by no signs of discomfort. This case affords evidence that, in adults, the morbid change can occur in a gradual and insidious manner, with no rheumatic nor other notable phenomena to mark its onset and progress. I have previously given many illustrations to show that a similar course is often manifested in the cases of children who come under treatment for the *consequences* of the cardiac lesion which has been so insidiously effected.*

* Clinical Lectures on Diseases of the Heart in Childhood: *Medical Times and Gazette*, Dec. 27, 1879, p. 711.

II. *Systolic Murmur at Apex becoming changed to Presystolic Murmur.*—The following notes are condensed from a report by my former house-physician, Dr. J. Needham, by whom the case was carefully watched. John W. D., aged eighteen, was admitted under my care at the London Hospital on October 17, 1877. Patient had had so little subjective symptoms that he said that, with the exception of chicken-pox, he had never been ill in his life until eight weeks ago. He had, however, been under treatment for *psoriasis* at intervals for nine years. His present illness was attended with pains in the limbs and abdomen. There was no effusion into the joints, and the temperature never rose above 100·2° Fahr. On admission a soft systolic murmur was noted in the mitral area, the outline of the heart, as determined by percussion, not differing from the normal. Two days after admission the systolic murmur was described as loud and conducted towards left axilla. Seven days after admission there was slight thrill at apex. Fifteen days after admission, the note says: "The cardiac conditions are considerably altered. There is now a well-marked thrill at apex, and, instead of the systolic murmur, there is a well-marked harsh murmur, increasing in intensity and terminated by a clear first sound. About two inches nearer the sternum a blowing systolic murmur is distinctly audible." The systolic murmur (which was in the tricuspid area) subsequently disappeared, and the presystolic became louder, terminating with a sudden uncomplicated first sound. The patient improved under treatment, but suddenly, six weeks after admission, became epileptic.

In this case there was no history of acute rheumatism, though probably the psoriasis was an indica-

tion of a rheumatic tendency. In other cases we have distinct evidence that the murmur of mitral regurgitation developed in relation with acute rheumatism may be, in course of time, accompanied by the murmur of mitral stenosis. We may take, as an example, the case of Lydia Grace P., a child of eight, admitted under my care at the North-Eastern Hospital in 1872. She suffered from acute rheumatism. Whilst under observation a systolic murmur developed at the apex. She was discharged convalescent, and readmitted in January of the following year with a second attack of rheumatic fever. There was now evidence of mitral regurgitation, with cardiac hypertrophy. She was again discharged convalescent, and readmitted on August 13, 1873, with a third attack of acute rheumatism. She now manifested well-marked *presystolic*, as well as systolic, murmurs at the apex. She was again discharged convalescent. I do not think it necessary to multiply examples—I have observed many such—of this mode of induction of the condition of mitral stenosis. I may add, however, that it would appear that in some cases the condition of regurgitation is *replaced* by that of stenosis. For example, in a child of nine (Elizabeth M.), a systolic bruit in July, 1869, was found to be accompanied by a presystolic in November; and two years afterwards a presystolic alone was audible, terminated by a sharp and loud impulse.

III. *A Presystolic Murmur developing insidiously may subsequently be found to be accompanied by a Systolic Murmur.*—Arthur V., aged eight, was admitted under my care at the North-Eastern Hospital for Children on December 30, 1874. He had never suffered from any definite disease, save measles and

whooping-cough at three years of age, but he had frequently been ailing. He manifested a highly pronounced presystolic thrill at the apex, and the presystolic impulse of the left auricle was easily demonstrated on the surface of the chest-wall. A well-marked presystolic murmur was abruptly terminated by the impulse of the ventricle. There was evidence of enlargement of the right chambers, but not of the left ventricle. On January 5 of the following year symptoms of subacute rheumatism were manifest, and then a systolic murmur became evident at the apex. Subsequently the systolic murmur increased in loudness, and was heard over a wide area, whilst the presystolic was only audible at a point just below and internal to the left nipple. Signs of want of compensation now became more marked, and œdema—which, however, disappeared under treatment—supervened. Such a history is by no means uncommon; the signs of regurgitation supervene on those of stenosis, and the double lesion becomes manifest.

I hope that the evidence which I have brought forward may enable us to see in a clearer light the mode of development of mitral stenosis. This evidence, as I consider, tends to show that in a considerable number of cases the origin and course are insidious and gradual. The disease is not independent of rheumatism, but is often unaccompanied by pronounced rheumatic phenomena; it is initiated by the form of endocarditis which I sketched in my first lecture as manifested by no subjective sign, accompanied by no prominent symptom, and yet differing in no essential feature from that which occurs in obvious relation with rheumatism. The endocarditis which results in mitral regurgitation is more violent, so to speak,

whilst that which initiates stenosis is more protracted, giving rise to a slower formation of fibrous, quasi-cicatricial tissue that under the even pressure of blood in the auricle tends to form the smooth septum which has erroneously suggested a possible congenital causation.

Not all the cases of mitral stenosis, however, originate in this manner. In some there has been first the induction, in association with the phenomena of acute rheumatism, of the lesion of mitral regurgitation; then has occurred probably a slow welding of the curtains; and in the repeated attacks of endocarditis the changes have been slower than those which result in retraction of curtains, cords, and columns to the ventricular wall.

By either of these modes produced, it is probable that secondary changes take place in the diseased tissue—under the tension of blood the fibrous septum thickens, for *it* has to bear the chief strain of the auricular pressure, and not the ventricle, as in the case of mitral regurgitation. In some cases it undergoes calcareous degeneration, and probably in others, where gouty signs are manifest, it becomes infiltrated with the earthy lithates.

Compensation in cases of mitral stenosis may be maintained, as in mitral regurgitation, for long periods. It may be even more simple in the former case than in the latter, for it is only a hypertrophy of the right ventricle, and not of both ventricles, that is needed to sustain it. The left ventricle, not being dilated, continues to afford a sufficient *point d'appui*, and it only needs the *vis à tergo* of a strong right ventricle, aided by a hypertrophied (or at least not enfeebled) auricle, to urge a sufficiency of blood

through the narrowed orifice. So long, therefore, as a good nutrition maintains the muscular power of right ventricle and left auricle, any special methods of treatment of a simple condition of mitral stenosis may be unnecessary. In course of time, however, the right ventricle or left auricle, or both, may begin to fail. Usually it is the former, but I have quoted a case in which it was markedly the latter, and in this I have no doubt the muscle failed on account of the great privations which the patient had undergone. The right chambers dilate on account of the pressure which is maintained within them if the compensatory muscular power begins to fail. Then ensue the dyspnœa, the œdema, ascites, &c., with which we are familiar in analogous cases of mitral regurgitation. To restore compensation we may use, for the most part, similar means to those which we have considered in regard to mitral regurgitation. When the gravest troubles of orthopnœa and dropsy have supervened, I have in many cases found that rest, combined with the administration of nutrients and tonics, and with digitalis, have restored the *status quo ut ante*, often for a considerable period.

Coincidently with the use of means for increasing muscular power, I consider that small and repeated abstractions of blood are even more valuable in mitral stenosis than in mitral regurgitation. The tension of the right heart may be sensibly relieved even by a leech or two applied over the præcordium. Dr. Bedford Fenwick has narrated a case which is an amusing as well as instructive example of the value of blood-letting in failure of compensation in mitral stenosis. A patient of Sir Andrew Clark, at the London Hospital, manifesting the physical signs of

mitral stenosis and aortic incompetency, had not improved by a month's treatment with rest, ether, senega, and digitalis. There occurred much dyspnœa, with signs of œdema of the lungs. The urine became scantier, the œdema increased, and coma appeared to be supervening. At this time the patient in his half-consciousness struck his own nose and brought on a copious epistaxis. Shortly after, consciousness returned, a copious diuresis followed during the night, and in less than a week the œdema disappeared, and the patient became convalescent. I quite agree with Dr. Bedford Fenwick that abstraction of blood by leeches or cupping is too much neglected in the cases we are considering, and that it is to be justified both by theory and practice.*

As regards the special action of *digitalis* in restoring compensation in cases of mitral stenosis, I am not convinced that this is so markedly proved to be beneficial as in the cases of mitral regurgitation. I have found that in some instances, as shown by the sphygmograph, digitalis has restored regularity, whilst in others it has increased irregularity of pulse. I believe it to be most valuable where stenosis and regurgitation are combined.

I am quite in accord with Dr. Broadbent, who has thus recently written: "In mitral incompetence digitalis may be given almost indefinitely, and patients often take it for years with obvious advantage, but such is not the case in mitral stenosis. Here the effects must be watched from day to day; at any time the action of the heart may all at once be disordered,

* On the Use of Venesection in Cases of Heart Disease, by Bedford Fenwick, M.D., M.R.C.P.: *Lancet*, Aug 5, 1882, p. 179.

many of its beats not taking effect on the systemic circulation, and failing to produce a pulse in the radial artery; the heart may be acting with fair regularity, and at the normal rate, when the pulse is rendered irregular in this way; or its rate may be slackened and its rhythm disturbed, the effects of which will be exaggerated in the pulse."*

Convallaria Majalis.—M. Sée has narrated three cases of mitral stenosis in which the extract of convallaria was administered. In the first there was a marked diuretic effect, the quantity of urine increasing under treatment from an average of one litre to two litres and a half and three litres, together with a great amelioration of the dyspnœa which was manifest on exertion. In the second case, evidencing œdema, ascites, and grave signs of cardiac failure, after a dose of one gramme per diem of extract of convallaria, marked diuresis occurred, and œdema disappeared in two days. Oliguria returned, and the dose was increased to one gramme and a half. In successive days the quantity of urine passed increased in the following proportions:—600 grammes, 2200 grammes, 2400 grammes, and 3000 grammes; it then fell to 2000 grammes, all signs of œdema and ascites having disappeared. The third case was one in which diabetes mellitus coexisted with mitral stenosis. In this case a very marked amelioration of the symptoms of imperfect compensation is recorded.

As in the cases of mitral regurgitation, I have endeavoured in those of mitral stenosis to place convallaria majalis on trial in as rigidly scientific manner

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* *International Journal of Medical Sciences*, Jan. 1886, p. 85.

as I could in the wards of a hospital. The following is a summary of the evidence:—

1. *Effects of Convallaria on the Excretion of Urine.* —These are shown in the following table.

TABLE V.—*Showing daily amounts of Urine, in ounces, in cases of Mitral Stenosis, treated by Convallaria Majalis.*

Case.	Before convallaria.	During convallaria.	After convallaria.
1	60 > 30 < 61 > 15 > 30	31 < 52 > 28 < 66 > 50 > 30	—
2	—	20, 15 < 55 > 40 < 90 > 80 < 115 > 100 > 50 > 4	14 < 34 < 42 < 92
2a	Readministration.	85 < 115 > 75	85 > 65
3	—	28 < 40 > 25 < 52 > 20 < 28 > 20	20 > 16 < 30 > 20
4	22 < 35 > 25	22, 38 > 35 > 25	25 < 40, 50 > 25, 30
5	—	20 < 42 > 28 < 60 > 34	—

It will be observed that in these cases of mitral stenosis convallaria exercised a pronounced diuretic effect. In all cases the quantity of urine was augmented during its administration. The influence is markedly shown in Case 2, wherein the daily amount excreted rose from 20 to 115 ounces, and on readministration from 85 to 115 ounces. After the maximum diuresis in this case there was a very scanty excretion—4 ounces. In most of the cases there was no oliguria at the end of the treatment, but the evidence here, as well as that in the cases of mitral regurgitation, renders it probable that the drug may, after the maintenance of a maximum blood-pressure in the renal arterioles, so constrict these as to impede the blood-supply. It will be well, therefore, with convallaria, as with digitalis, to suspend the

administration at intervals. It is a fair conclusion that convallaria is an important diuretic in cases of mitral stenosis, comparable in its effects with caffeine in mitral regurgitation, and that its effects in this direction are more pronounced in the obstructive than in the regurgitant lesion. We will now consider the cases of mitral stenosis in reference to the

Effects of Convallaria on the Pulse and Respiration.—In one case the pulse-rate progressively fell under ten-grain doses of the convallaria extract from 112 to 80, 76 and 72, and after suspension of the drug rose to 92, to again fall under digitalis to 70. In another case the pulse-rate which under ten-minim doses of tincture of digitalis had increased from 99 to 110, decreased under convallaria to 102 and 64, rising after the suspension of the drug to 72 and 120. The sphygmographic evidence is more valuable and more conclusive than the mere observation of the rate of the pulse. In a third case in which the conditions were very severe, there being tricuspid regurgitation with pulsating liver, the extreme irregularity of the heart was greatly altered for the better. The sphygmogram taken in the early period shows great irregularity and full dicrotism (Fig. 25, A); the second trace, taken after convallaria extract (ten-minim doses) for thirteen days, and tincture of digitalis for a subsequent thirteen days, shows a slow and almost regular pulse of fair tension (Fig. 25, B). The increase of arterial tension is well shown in another series of sphygmograms. Before the administration of convallaria the trace shows a scarcely perceptible tidal wave; there is great irregularity in time and volume, and there are frequent repetitions of the systole shown in the downward-sloping portions (Fig. 26, A).

After six days, tincture of convallaria in twenty-minim doses being administered three times a day, the tidal

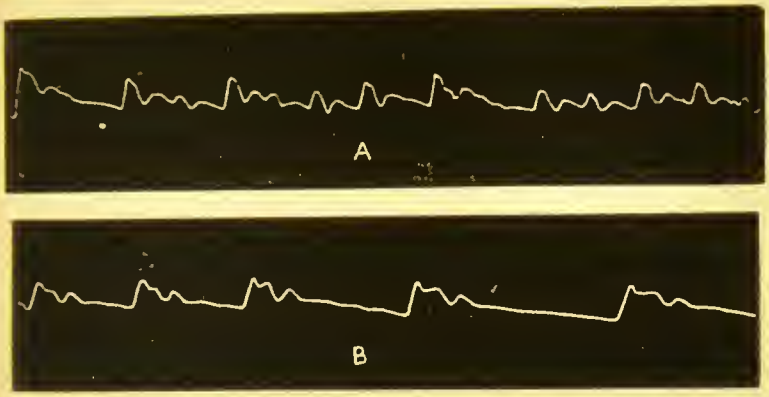

FIG. 25.—Sphygmograms in a case of mitral stenosis and regurgitation, with tricuspid regurgitation, treated by extract of convallaria, and subsequently digitalis. A, Before treatment; B, after treatment.

wave is seen to be much more marked, the summit of the trace being broadened, and there is much less

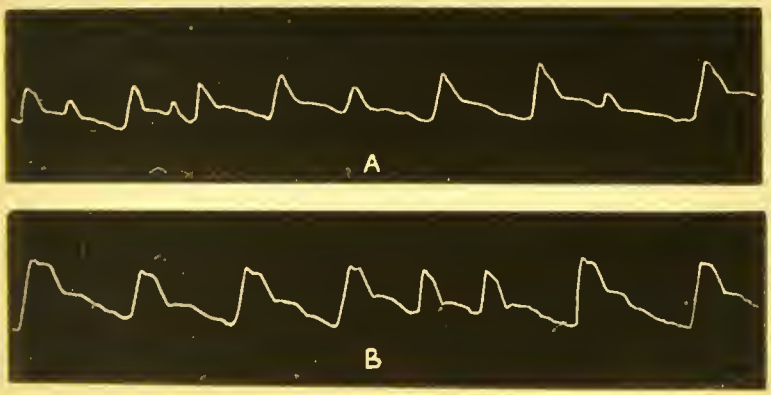

FIG. 26.—Sphygmograms in a case of mitral stenosis. A, Before the administration; B, after six days' treatment by twenty minims of tincture of convallaria taken three times a day.

irregularity (Fig. 26, B). The breathing was improved under the drug in nearly all the cases; in one case

there was severe dyspnœa, which lasted during a fortnight (in this case bronchitis and emphysema existed in marked degree), but afterwards there was gradual improvement, and the patient left the hospital free from all distressing symptoms. It was evident that in these cases the drug acted very favourably. Only one case died in hospital; in this pericarditis and severe pulmonary complications were manifested; the patient improved during the time that convallaria was administered, and the temperature was reduced from 101° to normal, but after the omission of the convallaria the temperature rose to 103°; the patient died suddenly after having for a time considerably improved.

So far as I have been able to judge, convallaria compares favourably with caffeine in the treatment of mitral stenosis. In one case a girl, aged seventeen, in whom there existed tricuspid regurgitation in addition to mitral stenosis and regurgitation, the quantity of urine rose from a maximum of 30 ounces before the administration of caffeine to a maximum of 59 ounces during its administration, and on re-administration from 30 ounces to 54 ounces; but in regard to the pulse and respiration there was no perceptible influence. In another case of stenosis with œdema, the daily urine rose only from 36 ounces to 40 ounces, and here also the pulse and respiration were not perceptibly influenced; the patient died. I was not encouraged to repeat the treatment by caffeine in the cases of mitral stenosis whilst I obtained such good results with convallaria; but in cases of this affection manifesting œdema or ascites, where a diuretic effect could not readily be obtained by convallaria, I should administer caffeine in addition.

My general conclusions are that caffeine is an agent of great value in the treatment of cases of mitral regurgitation, especially those in which there is much dropsy; and that convallaria, though manifesting no very favourable influence in cases of mitral regurgitation, except as an occasional substitute for digitalis, is of considerable therapeutic importance in mitral stenosis.

Considering the absence of violence in the storm which, involving the endocardium, leaves behind it the condition of obstruction, we may ask whether the result, stenosis, is not more innocent than the result of the more violent storm, regurgitation. The question is a difficult one. We can point to many cases of regurgitation where there has been an arrest of all morbid process, and where fair health has been maintained for long periods of years. Such instances are, I think, less common in mitral stenosis—there is not a like quiescence; and degenerative changes or intercurrent morbid phenomena are more likely to occur. The average age at death in nineteen cases of mitral stenosis observed by myself was thirty-five years. In forty-two fatal cases collected by the late Dr. Hayden it was 37·82 years.

In the cases both of mitral stenosis and of mitral regurgitation, however, it is not alone with the simple dynamical problem of the restoration of muscular compensation that we have to deal. In every case we have to weigh the probability of complications arising—complications so intimately associated with the conditions as to present an essential matter for consideration in any question as to treatment. Such are (1) repeated attacks of pericarditis or endocarditis, and (2) embolism.

A patient who has once suffered from rheumatic affection of the endocardium is liable, of course, to a repetition of the morbid process. With such pericarditis is by no means infrequently associated. In children I am strongly of opinion that pericarditis, when resulting in adhesion of the two layers of the pericardium (and often accompanied with fibrous proliferation amongst the muscular fibrils), is a grave cause of danger, spoiling the chance of compensation, and greatly interfering with the beneficial results of treatment. In cases of young people, where compensation fails even under suitable treatment and good nutrition, where evidences of cardiac hypertrophy and dilatation are in excess of those which usually accompany the valvular lesion, we may, I think, generally conclude that the pericardium is adherent.

An accident of the condition both of regurgitation and stenosis (especially the latter), yet intimately connected with them, is the occurrence of *embolism*. The consideration of this is often forced upon us when the question occurs as to treatment.

Let us consider this matter from its *clinical* aspect.

I. A case presents itself to us with symptoms of cough and dyspnœa. The onset of these symptoms has been sudden, perhaps initiated by a rigor. There may have been slight pyrexia or none. The characteristic feature is that, after a short time, when the cough has been attended with mucous and frothy sputa, the expectoration is observed to be coloured with bright blood. In many such instances we may find localized patches of dulness in the upper or the lower thoracic regions, with a few muco-crepitant râles; in others neither dulness nor moist sounds can be detected. We examine the heart, and find evidence

of mitral stenosis or (with less probability) mitral regurgitation. The existence of these signs, especially when the lesion is in the upper lobes, may cause us to fear the advent of pulmonary phthisis; but observation shows us that, though the hæmoptysis may occur again and again, the changes of tubercle are not manifest. Or whilst a case is under treatment for the symptoms of ill-compensated stenosis or regurgitation, a sudden attack occurs of dyspnœa with physical signs of a localized broncho-pneumonia. In some cases the outline of dulness can be delineated as a defined triangle. It is broncho-pneumonia differing from the ordinary form, for its origin may be entirely independent of causes operating from without, and it has a special feature—the occurrence of hæmoptysis. It is rarely that a case of mitral stenosis goes through its course without the manifestation of some such phenomena. Dr. Hayden records that hæmoptysis was noted as a symptom in forty-four cases out of eighty-one of mitral stenosis (54·3 per cent.). The history of fatal cases generally shows the repeated development of such areas of condensed lung. Morbid anatomy affords the clue to the interpretation of these phenomena. In many instances the right auricle is found to contain, adherent to its *musculi pectinati*, fibrinous coagula, and detached masses from these have been found to block branches of the pulmonary artery. From such infarctions result the appearances formerly described as "pulmonary apoplexy."* The infarct may in many cases be undiscoverable, for the plug undergoes fatty degeneration and solution, and

* Embolism of the pulmonary artery was found in eleven of sixty-eight fatal cases of cardiac disease of which I have records.

the lung-tissue may present no naked-eye changes. I am inclined to think, however, that what is true of the grosser is true of the finer changes, and that the hæmoptysis or the limited broncho-pneumonia of mitral stenosis is due to plugging (it may be of small twigs) of branches of the pulmonary artery.

Now as regards treatment when such phenomena are manifest. In the first class of cases, where no sign of ill-health has previously been prominent, I would accept the occurrence as evidence that compensation is disturbed. There is an abnormal retardation of the circulation in the right chambers of the heart, and we are called upon to use some of the means we have described for increasing the power of the ventricles. In all cases it will be advantageous if we can decrease the tendency to coagulation of the blood, even if we cannot promote the solution of that already coagulated. Dr. B. W. Richardson has advised the administration, in cases of fibrinous separation within the heart and vessels of the circulation, of large doses of ammonia (five-minim doses of the liquid ammonia in iced water or iced milk every half-hour in some cases). Where there has been imminent danger from pulmonary embolism I have employed this plan, and the patient has recovered. I think, therefore, that it is applicable in the cases of less imminent danger—of blockings with smaller coagula—which we are considering. Where, in mitral stenosis or mitral regurgitation, there are developed signs of broncho-pneumonia, I think it is advantageous to give ammonia, though it may not be in such heroic doses as those administered where there was danger of complete or extensive

plugging of the pulmonary artery. Professor Gerhardt advises carbonate of soda administered by inhalation.

II. The phenomena of embolism may be manifest on the *arterial* side of the circulation. As in the case of those which affect the venous, these may be observed (*a*) in patients who have not shown evidence previously of cardiac distress; (*b*) in those who are under treatment for cardiac disease. I have elsewhere* given ten examples of the sudden manifestation of lesions of the nervous system in patients who had never suffered from any rheumatic affection; and of these ten, six showed the signs of mitral stenosis. The nervous lesions were hemiplegia, hemianæsthesia, hemichorea, and epilepsy. In such cases there can be little doubt that fibrinous coagula detached from vegetations about the mitral orifice were carried by the current of blood, and blocked some of the arterial branches distributed to some part of the cerebro-spinal system.

Infarction in the wall of the intestine may give rise to peritonitis, and this must be considered as a possibility when symptoms referred to the abdomen occur in the course of cardiac disease. Infarcts have been found in the stomach, occasioning gastric ulcer. In the brain there may be single or multiple emboli. It is scarcely needful to say that in any case which manifests the signs of a sudden cerebral lesion the heart ought carefully to be examined. If valvular disease be shown to be in existence, rest and watchful care must be exercised; but it is by no means to be

* *Medical Times and Gazette*, Dec. 27, 1870, p. 712.

concluded that a severe or malignant form of endocarditis is in progress, for in many cases the lesions are recovered from. An opinion, however, on such a point must be given warily and only after repeated observations. Dr. Osler has shown that meningitis is a frequent complication of malignant endocarditis.

"In rare instances, the spinal meninges are involved and the clinical picture may be that of an acute cerebro-spinal meningitis." The cutaneous phenomena—purpura, patchy erythema, &c.—sometimes manifested in the course of rheumatic endocarditis, are probably, as was long ago pointed out by Virchow, instances of the effects of minute embolisms.

In cases under treatment for cardiac diseases, the one sign which I have found to indicate the probability of embolism is *a sudden rise of temperature* of the body. The locality of the embolism is not immediately indicated by the symptoms. The relative frequency of the sites of embolism, according to the returns from the Pathological Institute of Berlin, are—kidneys (75 per cent.), spleen (51), brain (20), intestinal tract and liver (7), skin (5), spinal cord (3), thyroid body and eye (occasionally). In my own cases the sites were—spleen (11 cases), kidneys (6), brain (5), retinal artery (1), intestines (1).

The occurrence of any of the phenomena of embolism in cases of valvular disease is an indication either of the recent development of endocarditis with the formation of vegetations, or of the detachment of an old vegetation, or of the occurrence of ulcerative endocarditis. In all cases the first essential for treat-

ment is the maintenance of *rest* and tranquillity of heart. The blood should be rendered as fluid and non-coagulable as possible, and to this end alkaline salts of ammonia or soda may be administered. The subject of the treatment of the secondary effects produced by the embolism—effects varying according to its site—of course I cannot approach on this occasion.

NOTE A.

Distribution of Micrococci in Ulcerative Endocarditis.—An interesting communication from Dr. Byrom Bramwell, illustrated by some admirable drawings (*The American Journal of the Medical Sciences*, for July 1886), demonstrates the distribution, by the blood current, of micrococci in ulcerative endocarditis, and their immigration into the tissues. In the case investigated well-marked cardiac murmurs, with variable temperatures and signs of embolism followed the division of a urethral stricture, perineal abscess being a complication. At the autopsy all the segments of the aortic valve were found to be covered with soft and luxuriant vegetations, in which micrococci were crowded in groups. One drawing shows a mass of micrococci contained within an artery dipping into the grey matter of the brain; the walls of the vessel are thickened, and micrococci are extruded into them. Other drawings show capillarics of the grey matter plugged with micrococci, and others ruptured with extravasated micrococci around them. The veins also contain abundant micrococci, which are also seen remote from the vessels in the brain-substance, in some portions intermixed with pus-cells and the products of inflammation. Further illustrations demonstrate enormous numbers of micrococci plugging some of the vessels of the Malpighian tufts of the kidney escaped into the intertubular tissue, scattered throughout the pyramidal portions, and invading the renal tubules. In the choroid coat of the eye groups of micrococci are seen in the midst of collections of pus-cells. In the skin, in the neighbourhood of a purpuric patch, groups of micrococci are figured in the layer below the epidermis, and in the wall of a small abscess in the subcutaneous tissue. It is needless to say that these observations illustrate, in a very important degree, the causal relations between micro-organisms and the lesions which attend ulcerative, or malignant, endocarditis.

NOTE B.

The Occurrence of Inflammation of the Tricuspid Valve in Ordinary Cases of Endocarditis. — Dr. Byrom Bramwell (*American Journal of the Medical Sciences*, April 1886, p. 419) considers that endocarditis involves the right side of the heart much more commonly than has been heretofore supposed. He bases this opinion partly on pathological and partly on clinical evidence. Deaths in the stage of recent endocarditis are comparatively infrequent, and therefore opportunity is not often afforded of examining the tricuspid valve at a period when inflammatory changes are in progress. In twenty-eight cases of recent simple endocarditis, vegetations were found on the tricuspid valve in fourteen—fifty per cent. of the recent cases, 16·86 per cent. of all the cases (83) of simple endocarditis examined. The conclusions arrived at are that acute inflammation of the tricuspid is of frequent occurrence in *acute* simple endocarditis, and that in severe cases of endo-pericarditis it is usually present; that chronic disease of the tricuspid, the result of endocarditis (as evidenced by the presence of cicatricial contraction of the valve-segments and the orifice), is of much less frequent occurrence; that (an inference from the two former propositions) acute inflammation of the tricuspid valve in many instances subsides, and is completely cured. In regard to clinical evidence, Dr. Byrom Bramwell believes that a systolic tricuspid murmur is the only sign by which right-sided endocarditis is, as a rule, manifested, and, from extant evidence, such a murmur is frequently developed in the early stages of acute rheumatism. I am obliged to demur to both these propositions. I have frequently shown to my class examples of chronic valvular disease, wherein pulsation of veins in the neck and pulsation of the liver have indicated tricuspid regurgitation, and yet no murmur has been audible in the tricuspid area. I have taught, therefore, that we must not rely alone upon the murmur as indicating regurgitation at the tricuspid orifice. Nevertheless, I am quite disposed to accept Dr. Byrom Bramwell's main conclusions. Not infrequently I have found, during the period when it is most probable that endocarditis is developing, a notable extension of præcordial dulness to the right

and a manifest pulsation of the veins at the root of the neck on the right side; yet, at a later period in the history of the case, both these signs have passed away. Such signs are, in my opinion, best explained by the theory of Dr. Byrom Bramwell, that an active endocarditis has been in existence in the right chambers, the fires of which have subsequently died out. Again, from the experience of the cases which I have observed, I cannot subscribe to the doctrine that a systolic murmur generated at the tricuspid aperture, is frequent in acute rheumatism attended with the development of endocarditis. Dr. Byrom Bramwell has quoted the statistics of the late Dr. Sibson, comprising 107 cases of acute rheumatism, in which endocarditis was present without pericarditis. A "tricuspid murmur" was present in fifty-one or fifty-two instances, 47 or 48 per cent. I must record my experience as widely different from this. I have very rarely observed a murmur whose origin I should distinctly locate at the tricuspid orifice in cases of acute rheumatic endocarditis. Our differences are probably differences of interpretation. The late Dr. Sibson seems to have defined a tricuspid murmur as "a murmur present over the right ventricle." I should probably consider this, in a large proportion of these cases, to be a murmur generated at the mitral orifice, but conducted towards the sternum. I do not recognize a murmur as tricuspid unless I can map out a distinct area of audibility over the situation at the base of the ensiform cartilage, or, supposing an apex murmur to be in existence, unless I can describe *two* areas of audibility or maximum—one about the left apex, the other over the tricuspid area. The question is too long to debate here. I can but record my opinion that of our means of detecting tricuspid regurgitation, the systolic murmur, heard in what is termed the tricuspid area, is the *least* reliable. Whether there be tricuspid murmur or signs of engorgement of the right side of the heart during the progress of rheumatic endocarditis, I am quite disposed to believe that such conditions are due to a wave of endocardial inflammation, and *not* to a passive dilatation, as was taught by the late Dr. Sibson. The arguments adduced by Dr. Byrom Bramwell in opposition to the so-called "safety-valve" theory, and to any theory which considers the engorgement of the right chamber to be a mere consequence of the affection of the left in *acute* endocarditis, I consider forcible and convincing. I entirely agree with Dr. Bramwell that these

views emphasize the importance of *rest* in the treatment of endocarditis. In his own words: "In treating cases of mitral endocarditis, our main object should be to imitate Nature's method of cure; to place the mitral valve, so far as we are able to do so, in the same condition as the tricuspid valve; in other words, to reduce the force (and also the frequency) of the cardiac contractions, and to allow the products of inflammation to be absorbed just as they are usually absorbed on the right side of the heart."

NOTE C.

A Cerebral Lesion in Exophthalmic Goitre.—Dr. Wm. A. Fitzgerald (*The Dublin Journal of Medical Science*, March 1 and April 2, 1883) discusses the question of the causation of the triple phenomena in Graves's disease, and adduces a large amount of evidence in favour of the view that the affection is due not to a morbid condition of the sympathetic, but to a lesion of certain centres in the brain. This theory has been forcibly enunciated by Sattler and Filehne. It is pointed out as a great difficulty in accepting the view that Graves's disease is the result of a cause operating directly upon the cervical sympathetic, that in such case we must assume diametrically opposite effects produced by the one nerve-lesion—for the exophthalmos, the vascular dilatations behind the orbit, the pulsations of the carotids, and the increase in bulk of the vessels of the thyroid gland, must be due to a *paralysing* influence upon the sympathetic, whilst the preternaturally increased cardiac action must be ascribed to an *irritating* effect upon the cardiac excito-motor portions of the same nerve. The theory advanced by Sattler is that in Graves's disease there is "a lesion of those circumscribed portions of the vaso-motor centre (or possibly of a still more central region of the brain) which preside over the vaso-motor nerves of the thyroid gland and of the intra-orbital tissues; and he infers, from the very great constancy with which the two symptoms of goitre and exophthalmos are found combined, that the portions in question must be situated exceedingly close together. The cardiac symptoms he ascribes to lesion of the cardio-inhibitory centre for the vagus." Von Graefe's sign—an impairment of the co-ordination of the movements of the upper eyelid and the globe, whereby

in the looking-downwards movement effected by the inferior rectus the lid fails to follow, but remains lifted owing to inhibition of the levator palpebræ or its tonic contraction—which is met with in a considerable proportion of the cases of this affection—is explained by the lesion of a definite co-ordinating centre for these special movements. Filehne brought the experimental method to the elucidation of the question, and succeeded in inducing the cardinal symptoms of Graves's disease in rabbits by wounding the *corpora restiformia*. Brown-Séquard had previously induced exophthalmos by wounding these bodies, and recorded the notable observation that the offspring of animals thus wounded manifested exophthalmos even through four generations.

Important as these considerations are, they do not afford us much help towards elucidating the questions of the etiology and treatment of the strange disorder. Assuming a lesion of such a limited portion of the brain, how is it produced? Again, how are the structural changes in the sympathetic ganglia which have been demonstrated in some cases, though not in all, to be explained? Is the lesion centrifugal?—are the nerve-changes in such cases descending changes? As regards proximate etiology, the cases which I have seen have appeared to me generally associated with troubles of the nervous system, with a severe mental shock, or with protracted trouble or sorrow. Mr. Jonathan Hutchinson says that the occurrence of the disorder in unmarried women and in *young* men, and its non-occurrence in pregnant women, suggest that it has some relation with the sexual functions. The discussion at the Ophthalmological Society on May 6, 1886 (*British Medical Journal*, May 15, 1886, p. 929), seemed to indicate that the disease in a considerable proportion of cases and in various modes of treatment tended towards recovery, partial if not complete. On the other hand, Dr. Samuel West stated that there were three deaths out of a total of thirty-eight cases collected by himself; and Dr. Carrington, that three fatal cases had occurred at Guy's Hospital during the last two years. It is strange that throughout the whole discussion no mention is made of the systematic employment of electricity as a method of treatment.

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